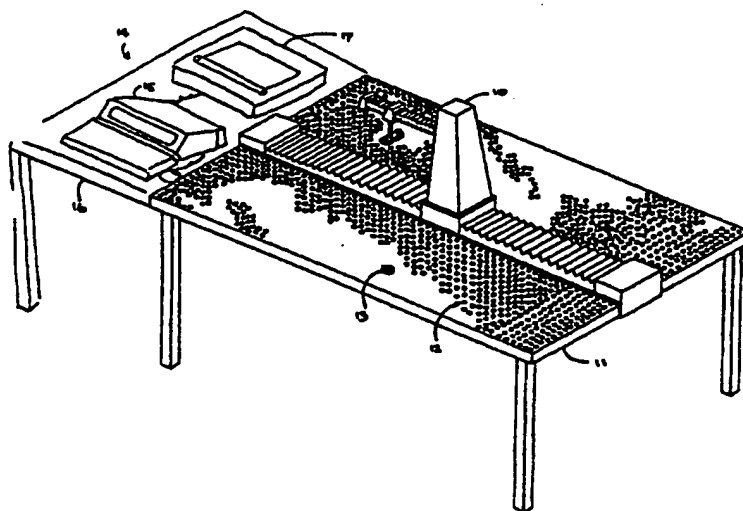




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<p>(21) International Application Number: PCT/US95/06156 (22) International Filing Date: 17 May 1995 (17.05.95) (30) Priority Data: 08/252,282 31 May 1994 (31.05.94) US (71) Applicant (for all designated States except US): BIOTEK SOLUTIONS, INCORPORATED [US/US]; 120-B Cremona Drive, Santa Barbara, CA 93117 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): BERNSTEIN, Steven, A. [US/US]; 2717 San Marcos Avenue, Los Olivos, CA 93441 (US). ERICKSON, Page, A. [US/US]; 2505 Calle Montilla, Santa Barbara, CA 93109 (US). BARKER, Stephen [US/US]; 143 Northridge Road, Santa Barbara, CA 93105 (US). (74) Agents: D'ALESSANDRO, Kenneth et al.; D'Alessandro & Ritchie, P.O. Box 640640, San Jose, CA 95164-0640 (US).</p>		<p>(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>

(54) Title: AUTOMATED TISSUE ASSAY USING STANDARDIZED CHEMICALS AND PACKAGES



(57) Abstract

A system which performs a plurality of independent analysis procedures simultaneously, possibly involving differing types of tissues and differing process steps, comprising a robotic arm (10), which may move the different tissue samples among a plurality of process stations (13), and a processor (15), which may select the next tissue sample to move, when to move it, and where to move it to. The processor may direct the robotic arm to interleave the differing process steps, adjust the process steps for conflicts, and optimize the order in which samples are moved. The processing stations may be disposed in a set of grid locations (12). The processing stations may comprise workstations for performing individual steps of the tissue assay procedures, such as solution trays. The processor may comprise a graphic interface by which an operator may specify the process steps, may monitor the progress of ongoing procedures, or override the determination of what process steps to perform.

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11
12 S P E C I F I C A T I O N

13
14
15 TITLE OF THE INVENTION

16
17 AUTOMATED TISSUE ASSAY USING STANDARDIZED CHEMICALS AND PACKAGES

18
19 CROSS-REFERENCE TO RELATED APPLICATION

20
21 This application is a continuation-in-part of
22 Application Serial No. 07/740,285 filed August 5, 1991, and
23 Application Serial No. 08/218,143, filed March 24, 1994, both
24 filed in the name of inventors Steven A. Bernstein and Page A.
25 Erickson, titled "Method and Apparatus for Automated Tissue
26 Assay", and assigned to the same assignee.

27
28 / / /

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to methods and apparatus useful in automated analysis or testing of tissue samples, and to automated tissue assay using standardized chemicals and packages.

2. Description of Related Art

The analysis of tissue is a valuable diagnostic tool used by the pathologist to diagnose many illnesses and by the medical researcher to obtain information about a cell structure.

In order to obtain information from a tissue sample it is usually necessary to perform a number of preliminary operations to prepare the sample for analysis. There are many variations of the procedures to prepare tissue samples for testing. These variations may be considered refinements to adapt the process for individual tissues or because a particular technique is better suited to identify a specific chemical substance or enzyme within the tissue sample. However the basic preparation techniques are essentially the same.

Typically such operations might include the processing of the tissue by fixation, dehydration, infiltration and embedding; mounting of the tissue on a slide and then staining the sample; labeling of the tissue through the detection of

1 various constituents; grid staining of tissue sections for
2 analysis by an electron microscope or the growing of sample cells
3 in culture dishes.

4
5 Depending on the analysis or testing to be done, a
6 sample may have to undergo a number of preliminary steps or
7 treatments or procedures before it is ready to be analyzed for
8 its informational content. Typically the procedures are complex
9 and time consuming, involving many tightly sequenced steps often
10 utilizing expensive and toxic materials.

11
12 These procedures must usually be performed in a
13 critical order for each sample and each treatment is frequently
14 time dependent. Additionally the laboratory is often under
15 extreme pressure to perform many different analysis as soon as
16 possible, entailing many different procedures and tests.

17
18 A sample of tissue may undergo an optical microscopic
19 examination so that the relationship of various cells to each
20 other may be determined or abnormalities may be uncovered. The
21 tissue sample must be an extremely thin strip of tissue so that
22 light may be transmitted therethrough. The average thickness of
23 the tissue sample or slice (often referred to as sections) is on
24 the order of 2 to 8 microns. A relatively soft and pliable
25 tissue such as might come from an organ of the human body, in its
26 fresh state cannot be accurately cut into such thin sections. In
27 addition, in order to see the individual constituents of the
28 cells, such as the nucleus, the nucleolus, the cytoplasm and the

1 cell membrane, it is preferable to have them colored by different
2 dyes to produce a contrasting appearance between the elements.
3 Very limited dye staining can be done on fresh or recently living
4 tissue without resorting to chemical processing. Typically a
5 sample of tissue 2.0 to 2.5 square centimeters in area and 3 to 4
6 millimeters thick is utilized. The tissue sample is then fixed
7 in a material (a fixative) which not only preserves the cellular
8 structure but also stops any further enzymic action which could
9 result in the putrefication or autolysis of the tissue. While
10 many substances can function as a fixative, a 4% formaldehyde or
11 a 10% formalin solution is very common. Other common fixatives
12 would include ethanol, picric acid or mercuric chloride usually
13 with formalin. It should be remembered that in dealing with
14 these substances the containers holding the materials must be
15 suitable. For example mercuric chloride severely corrodes metals
16 and therefore should normally be contained in a glass vessel.

17
18 To prepare good samples for microscopic examination the
19 initial step should kill the enzymic processes of the tissue and
20 should alter or denature the proteins of the cell through
21 fixation. The period of fixation may take several hours or even
22 a few days depending upon the tissue type, sample size and type
23 of fixative being used.

24
25 After fixation, the tissue sample is often dehydrated
26 by the removal of water from the sample through the use of
27 increasing strengths of alcohol or of some other dehydrating
28

1 fluid. Gradual dehydration is preferred because it causes less
2 distortion to the sample than a rapid dehydration process.

3
4 The alcohol is then replaced by a chemical which mixes
5 with wax or some other plastic substance which can permeate the
6 tissue sample and give it a consistency suitable for the
7 preparation of thin sections without disintegration or splitting.
8 Fat solvents, such as chloroform or toluene are commonly used for
9 this step. The sample, which has been dehydrated by the
10 infiltration of alcohol, is next exposed to several changes of
11 solvent over a period that may last from a few hours to days
12 until the alcohol is completely replaced by the solvent. The
13 sample is then exposed to a wax which is soluble in the solvent.
14 If a paraffin type wax is used the infiltration is at a
15 temperature above its melting point. After the wax infiltration
16 the sample is allowed to cool and the wax solidify so that the
17 sample is entirely embedded in and infiltrated by the wax.

18
19 A microtome is then utilized to cut thin slices from
20 the tissue sample. The slices are on the order of 5 to 6 microns
21 thick. The cut thin sections are floated on water to spread or
22 flatten the section. The section is then disposed on a glass
23 slide, usually measuring about 8 by 2.5 millimeters.

24
25 The wax is then removed by exposing the sample to a
26 solvent, the solvent removed by alcohol, and the alcohol removed
27 by decreasing the alcoholic concentrations until eventually the
28 tissue is once more infiltrated by water. The infiltration of

1 the sample by water permits the staining of the cell constituents
2 by water soluble dyes.

3
4 Prior to the development of automated procedures for
5 the preparation of tissue samples, it often took from 2 to 10
6 days before the tissue could be examined under a microscope. In
7 more recent years automated processes have been developed
8 utilizing apparatus to transfer the sample from one fluid to
9 another at defined intervals, and as a result the preparation
10 time has been significantly reduced to between about 4 and 16
11 hours.

12
13 Variations in the materials used in the preparation of
14 the sample are advantageous under some circumstances. The use of
15 ester wax allows sections 1 to 3 microns thick to be cut with
16 less contraction than that which occurs when paraffin used. The
17 sample is exposed to higher temperatures when paraffin wax is
18 used. The use of cellulose nitrate embedding shrinks tissues
19 less than wax, produces good cohesion between tissue layers and
20 permits large undistorted sections to be cut 25 to 30 microns
21 thick, if so desired. It is clear that persons with skill in the
22 art of tissue preparation may use many different materials to
23 which the samples may be exposed.

24
25 Tissue staining is a procedure which is utilized to
26 make microscopic structures more visible. Perhaps the most
27 common stain materials are hematoxylin and eosin. Hematoxylin is
28 utilized to clearly stain the nuclei of cells dark blue. Eosin

1 is used to stains the cell cytoplasm various shades of red or
2 yellow, presenting a clear contrast to the blue stain of the
3 nuclei.

4
5 Many synthetic dyes are derived from benzene which is
6 colorless but by changing its chemical configuration color
7 compounds are produced which are called chromophores. It is
8 these chromophores which constitute the bulk of the different
9 coloring dyes used in research and routine histology.

10
11 There are many techniques by which sample tissues may
12 be stained and most of these techniques require exposing the
13 sample to various solutions. Histochemistry is the science by
14 which chemical reactions are used to identify particular
15 substances in tissues. In addition, many enzymes can be detected
16 by exposing a sample to a particular chemical substance on which
17 the enzyme is known to have an effect such as turning the
18 substance into a colored marker. Thus from the above it can be
19 seen that a sample tissue may be exposed to various antibodies,
20 enzyme labeled detection systems, colormetric substrates,
21 counterstains, washing buffers and organic reagents.

22
23 Many experimental and observational research projects
24 involve experimentation to authenticate new techniques and these
25 experiments can be very extensive and time consuming.

26
27 In addition to the techniques that prepare samples for
28 optical microscopy, techniques often must be utilized which make

1 the use of electron microscopes suitable in the examination of
2 tissue samples. Actually it has been found that the pathological
3 examination of almost any disorder makes electron microscopy
4 highly desirable and often essential.

5
6 Tissue samples for use with an electron microscope may
7 be fixed in glutaraldehyde or osmium tetroxide rather than in the
8 standard fixatives used for optical microscopy samples. Usually
9 very small samples of tissue are embedded in methacrylate or
10 epoxy resin and thin sections are cut (about .06 microns thick).
11 Staining is most often done by colored solutions and not dyes,
12 and heavy metal salts are utilized to enhance contrasts of
13 density.

14
15 From the above brief description of some of the
16 techniques and materials used by a pathologist in the examination
17 of tissues, it can be seen that for a research laboratory to
18 carry out such a wide variety of processes and numerous different
19 tests assisting apparatus would be desirable and almost
20 mandatory. Other and further information about tissue analysis
21 and tissue assays may be found in the following references, each
22 of which is hereby incorporated by reference as if fully set
23 forth herein:

24
25 Bancroft, J.D. and A. Stevens. Theory and Practice of
26 Histological Techniques (3rd ed. 1990). Churchill
27 Livingstone: Edinburgh. ISBN 0-443-03559-8.

28

1 Childs, G.W. Immunocytochemical Technology (1986). Alan R.
2 Liss, Inc.: New York. ISBN 0-8451-4213-5.

3
4 Culling, C.F.A., R.T. Allison and W.T. Barr. Cellular
5 Pathology Technique (4th ed. 1985). Butterworths: London.
6 ISBN 0-407-72903-8.

7
8 Sternberger, L.A. Immunocytochemistry (2nd ed. 1979). John
9 Wiley & Sons: New York. ISBN 0-471-03386-3.

10
11 Many pathology laboratories have in fact automated many
12 of the simple and routine procedures described above such as
13 simple staining or sample embedding. Where the same procedure is
14 repeated with great frequency, laboratories have often designed
15 specialized machines to perform the often repeated testing
16 simultaneously on many samples. Typical of such machines are the
17 equipment used in the routine analysis of blood samples. The
18 equipment used in this type of laboratory is capable of treating
19 multiple samples simultaneously to the same testing procedure,
20 i.e., parallel testing or through the use of multiple machines
21 the same result of parallel testing, is achieved. Alternatively
22 the laboratory may perform the same test repetitively, i.e.,
23 sequentially and thus subsequent samples may be subject to a
24 significant time delay.

25
26 Research laboratories often are required to perform
27 non-routine analysis requiring many different test procedures.
28 As a result of this lack of repetitive procedures, research

1 laboratories have relatively little automated equipment to assist
2 the researchers in their task. The most obvious reason for this
3 lack of automation is that the equipment presently available is
4 dedicated to a limited number of procedures most commonly
5 performed. The equipment is not flexible enough to permit a wide
6 variety of operations to be easily accomplished nor does the
7 present equipment permit easy and facile changes to the
8 operations.

9
10 Another problem that has arisen in the art of repeated
11 testing is that of reagent supply. Typically, devices to perform
12 repeated testing must be loaded with bulk reagents, and those
13 bulk reagents must have sufficient volume that a specimen slide
14 can be immersed in the reagent, at least to the level of the
15 specimen. This can be wasteful of expensive reagents. It can
16 also result in substantial contamination with the reagent of the
17 back or sides of the slide, resulting in significant carryover of
18 the reagent and its chemical effect into a next step, and a
19 possible safety hazard for the operator or support personnel.

20
21 Another problem that has arisen in the art of repeated
22 testing is that of packaging of reagents for tests. Typically,
23 devices to perform repeated testing comprise isolator pads,
24 essentially hydrophobic surfaces of glass or plastic, with
25 roughened areas to contain the reagent and smooth areas to repel
26 it. This can cause two problems. First, if too much of the
27 reagent is doled out by the operator, it can overflow the
28 isolator pad and mix with another reagent. Second, the reagent

1 has a near maximal surface/volume ratio, often resulting in
2 significant evaporation of the reagent before use.

3
4 SUMMARY OF THE INVENTION

5
6 The invention provides a system which performs a
7 plurality of independent analysis procedures simultaneously,
8 possibly involving differing types of tissues and differing
9 process steps. The system comprises a robotic arm, which may
10 move the different tissue samples among a plurality of processing
11 stations, and a processor, which may select the next tissue
12 sample to move, when to move it, and where to move it to. In a
13 preferred embodiment, the processor may direct the robotic arm to
14 interleave the differing process steps, for example by time
15 division multiplexing.

16
17 In a preferred embodiment, the processing stations may
18 be disposed in a set of grid locations, so that the location of
19 any one processing station may be specified by an X coordinate
20 and a Y coordinate, and possibly a Z coordinate for height. The
21 robotic device may comprise a bench robot with sufficient degrees
22 of freedom that it is able to reach each of the grid locations
23 with suitable movement. The processing stations may comprise
24 workstations for performing individual steps of the tissue assay
25 procedures, such as solution trays, or other equipment useful in
26 bioassay, biomedical or related environments.

27
28

1 In a preferred embodiment, the processor may select a
2 tissue sample to be moved in response to timing information about
3 the procedures, which may specify a time duration range (e.g., a
4 minimum time and maximum time) each process step should take.
5 The processor may determine the exact time for a step by
6 generating a possible sequence of steps and examining that
7 sequence for conflicts, adjusting that sequence in response to
8 those steps with a specified range of times, and iterating the
9 calculation over a plurality of possible sequences. The
10 processor may also optimize the order in which samples are moved
11 to minimize the total time required by the system to complete the
12 procedures, for example by generating a plurality of possible
13 sequences, evaluating each sequence for total expected time, and
14 selecting the best sequence available.

15
16 In a preferred embodiment, the robotic device comprises
17 a set of standardized packages, disposed by means of a set of
18 spring locks on a set of standardized tiles and accessed by a set
19 of standardized holders for standardized slides or slide pairs,
20 having contents comprising a standardized reagent, chemoactive or
21 bioactive compound or mixture, or buffer, and a set of
22 preprogrammed assay protocols. A standardized workstation may
23 also comprise another type of device for operating on sample
24 slides (or other carrying media such as test tubes or wafers),
25 such as a centrifuge, diffusion, distillation or other separation
26 device, a DNA crosslinking device, an electroporator, a microwave
27 device or other radiation source, an incubation oven or other
28 heating unit, or a refrigeration element or other cooling unit.

1 Because the packages, tiles, contents, and protocols are
2 standardized or preselected, the operator may quickly insert the
3 packages into the tiles, open the packages for operation, and
4 select a preprogrammed assay protocol. All these operations may
5 be performed quickly and may promote rapid and efficient
6 operation of the robotic device.

7
8 In a preferred embodiment, the processor may comprise a
9 graphic interface by which an operator may specify the steps of a
10 procedure. A display of the grid locations may comprise symbols
11 for the workstations, which an operator may identify with a
12 pointing device such as a mouse. The operator may create or edit
13 templates for workstations, create or edit lists of process steps
14 for procedures, monitor the progress of ongoing procedures, or
15 override the determination of what process steps to perform. For
16 example, in a preferred embodiment, the operator may create a
17 list of process steps for a procedure by selecting a sequence of
18 workstations with the mouse, and associating timing or other
19 information for each process step with the selected workstation.
20 The operator may also choose to select a stored list of process
21 steps for a procedure.

22
23 Thus, the invention provides apparatus and methods
24 whereby a plurality of test procedures can be performed on
25 several samples, e.g., through the use of time division
26 multiplexing. The invention also provides apparatus for use in a
27 laboratory for assisting in the performance of multiple tests
28 which can be easily programmed by the operator to execute

1 sequentially timed step procedures for a plurality of test
2 samples. The invention also provides a flexible laboratory
3 testing system which may use time division multiplexing to
4 interleave the multiple steps of a plurality of test procedures
5 to allow for a plurality of different procedures to be performed
6 on several different test samples in parallel.

7
8 BRIEF DESCRIPTION OF THE DRAWINGS

9
10 Figure 1 shows a robotic device for use with the
11 invention.

12
13 Figure 2 shows a laboratory setup having robotic
14 equipment like that shown in figure 1.

15
16 Figure 3A shows a standardized tile for coupling to the
17 robotic device.

18
19 Figure 3B (comprising 6 parts, individually figures 3B-
20 1, 3B-2, 3B-3, 3B-4, 3B-5, and 3B-6) shows a standardized package
21 for coupling to the tile.

22
23 Figure 3C (comprising 3 parts, individually figures 3C-
24 1 and 3C-2, and multiple page figure 3C-3) shows first and second
25 standardized slide holder for coupling slides to a compound or
26 mixture in a package.

1 Figure 3D (comprising 2 parts, individually figures 3D-
2 1 and 3D-2) shows a workstation having an incubation oven and a
3 carrying medium for inserting slides or slide pairs.

4
5 Figure 3E is a flowchart of a preferred method of
6 operating the robotic system with standardized packages and
7 contents.

8
9 Figure 4 is a flowchart showing a time line for five
10 tasks.

11
12 Figure 5 is a flowchart illustrating multitasking of
13 the tasks shown in Figure 4.

14
15 Figure 6 shows a multitask monitoring screen as viewed
16 by an operator.

17
18 Figure 7 shows a template building screen as viewed by
19 an operator.

20
21 Figure 8 shows a process building screen as viewed by
22 an operator.

23
24 Figure 9 shows a process timing screen as viewed by an
25 operator.

26
27 / / /
28

DESCRIPTION OF THE PREFERRED EMBODIMENT

Inventions described herein may be made or used in conjunction with inventions described, in whole or in part, in the following patents, publications, or copending applications, all of which are hereby incorporated by reference as if fully set forth herein.

U.S. Patent Application Serial No. 07/740,285, filed August 5, 1991, in the name of inventors Steven A. Bernstein and Page A. Erickson, titled "Method and Apparatus for Automated Tissue Assay"; and

U.S. Patent Application Serial No. 08/218,143, filed March 24, 1994, in the name of inventors Steven A. Bernstein and Page A. Erickson, titled "Method and Apparatus for Automated Tissue Assay".

In a preferred embodiment, a multiple axis bench top robot is located to reach peripheral auxiliary equipment disposed in the operational area of the robot. The robot may respond to the output of a PC type computer which utilizes process control programs and assay development software. Peripheral equipment, a plurality of work modules or workstations, is disposed in a grid like pattern around the bench top robot. The workstations may be disposed or arranged in any convenient pattern and may be represented by a template. Each grid location may contain the

1 necessary equipment to perform a single step of a tissue assay
2 procedure.

3
4 For example, a workstation at a grid position may
5 contain a solution tray into which one or more slides may be
6 immersed by the robotic equipment. The slide, or slides, could
7 be immersed to a predetermined depth and retained in the solution
8 tray for a precise time. It should be clear that each grid
9 location may have a solution tray having different depths or
10 different dimensions. Alternatively, a grid location could
11 contain a slide holder or other peripheral equipment capable of
12 performing a single function on the sample.

13
14 The robotic equipment or robotic arm may be controlled
15 by a standard PC computer. The assay development software is
16 graphic in nature and places a model of the peripheral grid on
17 the screen of the computer. While each tissue assay may have all
18 its steps preprogrammed the assay development software permits
19 the steps of the procedure or the timing of the steps to be
20 altered. The graphic nature of the presentation permits
21 laboratory personnel to alter such elements without the necessity
22 of relying on a computer or programming expert.

23
24 The process control software associated with the PC may
25 monitor the progress of the assays, may permit manual override of
26 an automatic operation, and most importantly, may permit
27 scheduling of multiple assays simultaneously in parallel through
28 the use of time interleaving of the various steps in the test

1 procedures. Thus while sample #1 may be disposed at a
2 workstation in a grid location where it undergoes a drying
3 operation, sample #2 may be located in a tray containing a
4 staining solution while sample #3 is undergoing a fixation step.
5 The timing of each step is accurate and the system interleaves
6 the steps and utilizes the "waiting" or processing time between
7 steps in a single procedure to perform operational steps on other
8 samples which may be undergoing completely different preparation.

9 10 LABORATORY BENCH AND ROBOTIC DEVICE

11
12 Figure 1 shows a robotic device for use with the
13 invention. Figure 2 shows a laboratory setup having robotic
14 equipment like that shown in figure 1. The equipment may include
15 a robotic device 10 mounted on a standard laboratory bench top
16 11. The bench top 11 defines the operational area reachable by
17 the robotic device 10. The bench top 11 may have integral
18 therewith a plurality of locating elements such as holes 12.
19 Alternatively, the locating elements may be disposed on a
20 separate base disposed between the robotic device 10 and the
21 laboratory bench top 11. A template may be used to represent the
22 operational area and to assist in defining the exact location of
23 each workstation.

24
25 Located on the bench top 11 are one or more work
26 modules 13. A control station 14 is located adjacent to the
27 laboratory bench 11. The control station 14 may include a
28 typical PC type computer 15, such as an IBM-compatible computer

1 having an Intel x86 processor, or a computer similar thereto,
2 mounted on a desk 16 or other working surface. It would be clear
3 to one of ordinary skill in the art, after perusal of the
4 specification, drawings and claims herein, that other types of
5 computers may be utilized to control the movement of the robotic
6 arm 10. A printer 17 is shown although other peripheral
7 equipments may be utilized in conjunction with the computer 15.

8
9 Referring to the bench top 11, a plurality of locating
10 holes 12 are disposed at predetermined fixed locations relative
11 to the robotic device 10. The locating holes are designed to
12 receive modular workstations 13. Each modular workstation 13 is
13 designed to be used in the performance of a particular process or
14 step in one laboratory task or test procedure. Thus each
15 function required to be performed in a task is associated with a
16 work module 13 which has a predisposed known position on the work
17 bench 11.

18
19 There are a number of methods by which the location of
20 a particular work module 13 can be supplied to the computer 10.
21 For example each work module 13 may include a floppy disk which
22 would contain the physical characteristics of the work module,
23 such as its height, width and length. The customized data for
24 each module would be fed into the central processing unit of the
25 computer and would query the operator, for example through a CRT
26 display, to provide the location of the work module. The
27 operator through the keyboard input would specify the location of
28 the module on the locating grid. Thus for each work module or

1 step of a task the computer would have stored in its memory the
2 physical characteristics and location of the module.

3
4 In a preferred embodiment, the robotic device 10 is
5 capable of travel in an X direction along a first cable driven
6 bearing 20 (actuated by a first cable drive 20a). Disposed at
7 right angle to and vertical with respect to the first cable
8 driven bearing 20 is a second cable driven bearing 21 (actuated
9 by a second cable drive 21a), capable of traversing the first
10 cable drive 20a. Coupled to the cable drive 21a is a third cable
11 driven bearing 22 (actuated by a third cable drive 22a) disposed
12 at a right angle. A robotic hand 23 is mounted on cable drive 22
13 and comprises a spring loaded solenoid 23a coupled to a rubber
14 securing ring 23b. The securing ring 23b is capable of coupling
15 to a sample carrier 23c. The sample to be assayed (which may be
16 a tissue sample) is mounted on the sample carrier 23c.

17
18 Thus the hand 23 on which the sample is mounted is
19 capable of X movement along cable driven bearing 20, Y movement
20 along cable driven bearing 21, and Z movement along cable driven
21 bearing 22. The system illustrated is thus capable of motion
22 relative to three axes. Although the system is illustrated using
23 cable driven bearings 20, 21 and 22, it would be clear to those
24 skilled in the art, after perusal of this application, that other
25 robotic equipment could be provided that could decrease or
26 increase the number of axes, that other techniques other than
27 cable drives and cable driven bearings, (such as lead screws,
28 gears, belts, or other devices) could be used, that such other

1 equipment or techniques would be workable, and are within the
2 scope and spirit of the invention.

3

4 Typically, the range of movement along the X axis may
5 be about 76 inches, along the Y axis about 19 inches, and along
6 the Z axis about 18 inches. Such a typical range of movement
7 could provide approximately 15 cubic feet of operational area.

8

9

SYSTEM OPERATION

10

11 In order to illustrate the operation of this invention,
12 let it be assumed that the laboratory has five example tasks to
13 accomplish, each having five example steps. For purposes of
14 illustration, the five steps in each of the five tasks will be
15 utilized to demonstrate the multitasking capabilities of the
16 invention. The five tasks and the five steps of each of the
17 tasks are shown in Table 1 herein.

18

19 It is apparent from Table 1 that some of the tasks
20 utilize the same steps such as Pad 1 or Buffer 1. If these steps
21 were to be carried out in accordance with the principles of this
22 invention, it would be necessary to provide only 14 work modules
23 even though 25 steps were being performed. Disposed on the grid
24 would be a separate work module for each of the 14 different
25 steps listed above. Thus there would be a Pad 1 module to be
26 used in carrying out seven of the above steps. Alternatively,
27 the user could provide multiple modules, each capable of
28 performing the pad function. A Buffer 1 module would be used for

Task #1	Basic Fuchsin Staining
Step #1	Buffer 1
Step #2	Buffer 2
Step #3	Basic Fuchsin
Step #4	Pad 1
Step #5	Buffer 2
Task #2	Azure II & Methylene Blue
Counterstaining	
Step #1	Azure II
Step #2	Pad 1
Step #3	Buffer 1
Step #4	Pad 1
Step #5	Methylene Blue
Task #3	Tissue Fixation
Step #1	Isotonic Rinse
Step #2	Primary Fixative
Step #3	Buffer 1
Step #4	Buffer 2
Step #5	Secondary Fixative
Task #4	Immunocytochemistry
Step #1	Buffer 1
Step #2	Pad 1
Step #3	Blocking Antibody
Step #4	Pad 1
Step #5	Buffer 1
Task #5	Slide Silinizing
Step #1	APTES
Step #2	Toluene
Step #3	Water
Step #4	Pad 1
Step #5	Oven

five of the steps and a Buffer 2 module for two of the steps. Each of the remaining steps would have a module disposed on the grid to perform the necessary work associated with the step.

It is often essential that the step of the task be performed within certain time limits. The timing of some steps can be critical. Figure 4 is a flowchart showing a time line for the five steps of the tasks in Table 1. It should be noted that Task #1, Step #1 commences at 9:00 and has a duration of

1 approximately 15 minutes, inclusive of the time necessary to
2 transport the sample to the location where Step #2 is performed.
3 Thus Step #2 will commence at approximately 9:15. It should be
4 noted that the timing for the start of Step #2 has some leeway in
5 that it can commence between 9:15 and 9:18, providing leeway of
6 three minutes. Step #2 has a duration of approximately 11
7 minutes and the sample is transported to the location where Step
8 #3 will be performed. The time for performing Step #3 is
9 critical as indicated by the lack of interval for the starting
10 times. Step #3 must commence at 9:26. Fourteen minutes later
11 the sample is undergoing Step #4, which can commence any time
12 between 9:40 and 9:50. The last Step #5 is performed at 9:51.
13 It should be noted that if each Step is commenced at the outer
14 time limit Step #5 may not begin until 10:22.

15
16 In a similar manner it can be determined from figure 4
17 that the five steps of Task #2 may consume 1 hour 34 minutes,
18 Task #3, 1 hour 9 minutes, Task #4, 1 hour 17 minutes, and Task
19 #5, 1 hour 16 minutes. Thus if the five steps of the tasks shown
20 were to be performed sequentially the total time to completion
21 would be 6 hours 38 minutes.

22
23 Referring to figure 5, the multitasking method of this
24 invention is therein illustrated to show the time interleaving of
25 the steps of the multiple tasks. Assuming again for purposes of
26 illustration and simplification of explanation that we are
27 desirous of performing the same five steps for the same five
28 tasks. Under the control of the computer the robotic hand would

1 be commanded to obtain sample #1 or alternatively the sample
2 could be brought to the robotic hand and for grasping. The hand
3 retaining the grasped sample would move the sample to the
4 location of the work module for Task #1, Step #1, i.e., Buffer 1.
5 The sample would be freed from the hand and left at the work
6 module. The hand would proceed to the location of sample #2
7 where it would grasp the sample and carry it to the work station
8 where Task #2, Step #1 would be performed.

9
10 Each of the five samples would in turn be grasped by
11 the robotic hand and transported to the work module associated
12 with the first step of the task to be performed on each sample.
13 It should be noted that the design of the Buffer and Pad work
14 modules permit the simultaneous treatment of at least two samples
15 from different tasks. Alternatively, two work modules could be
16 provided so that each sample could be treated in a different
17 module.

18
19 After locating sample #5 in the Task #5, Step #1
20 module, the robotic hand returns to the module for Task #5, Step
21 #1 and grasps the sample #5 and transports it to the module for
22 Task #5, Step #2. Following the path illustrated in figure 5,
23 the hand proceeds from the Task #5, Step #2 module to Task #3,
24 Step #3 module where it grasps sample #3 and transports it to
25 Task #3, Step #2 module where the sample is deposited. The hand
26 then returns to the location of the first sample which is in the
27 module associated with Task #1, Step #1 and takes it to the
28 module for Task #1, Step #2. The hand returns to the location

1 sample #4 and carries it to Task #4, Step #2 and then at the
2 appropriate time transports the same sample to Step #3 of Task
3 #4.
4

5 At this point in the operation of the system, the
6 computer detects that Task #1, Step #3 and Task #2, Step #2 are
7 both scheduled to start at the same time, 9:26. In order to
8 resolve the conflict the system utilizes a technique, herein
9 termed "fuzzy timing", to process the control of the robotic hand
10 and optimize the process. Fuzzy timing may comprise the window
11 of time during which each process (Task) step may occur without
12 affecting the process results. Some steps of a process may be
13 critically timed, i.e., the time required for that step is exact,
14 such as Task #1, Step #3 in figure 5, but in general most steps a
15 process the timing is less critical and may comprise any amount
16 of time within a known range and thus are noncritical in their
17 timing, such as Task #2, Step #2, which has a window of four
18 minutes, as shown in figure 5. The system of this invention uses
19 these windows of time to advantage as to optimize (minimize) the
20 time necessary to complete the multiple tasks.
21

22 The use and advantages of "fuzzy timing" can be
23 illustrated by considering two different tasks, each having a
24 process step terminating at the same time or within moments of
25 the another. Assuming that both steps are critically timed in so
26 far as the termination time is concerned, it is apparent that
27 both samples from the two different steps can not be moved to the
28 next step in each process simultaneously since concurrent

1 movement of two samples is not within the capabilities of this
2 embodiment. Thus it is necessary to adjust the starting times
3 for the two steps relative to each other so that the ending times
4 will allow for the movement of each sample to its next process
5 step. While this can be done quite easily, it is clear that the
6 mere adjustment of a starting time for a step in the process may
7 well cause other timing conflicts. It is possible that under
8 such conditions the system could not support simultaneous
9 throughput of multiple processes unless the timing was altered.

10
11 Fuzzy timing allows the system additional flexibility
12 since by providing a window of time at each noncritically timed
13 process step, conflicts will be minimized through the adjustment
14 of timing at the step level, rather than by shifting the timing
15 of the whole process or task.

16 17 STANDARDIZED CHEMICALS AND PACKAGES

18
19 Figure 3A shows a standardized tile for coupling to the
20 robotic device.

21
22 As described herein, the robotic device 10 may be
23 mounted on a bench top 11 having a plurality of locating elements
24 such as holes 12 and having a plurality of work modules 13
25 disposed thereon.

1 In a preferred embodiment, each work module 13
2 comprises one or more tiles 301, each tile 301 comprising a
3 molded plastic piece having a top face 302 and a bottom face 303.
4

5 The bottom face 303 of the tile 301 comprises a
6 relatively flat plastic surface 304, possibly having one or more
7 bottom indentations 305 and bottom ribs 306, and having a set of
8 receiving wells 307 for insertion of a corresponding set of
9 fasteners 308. As shown in figure 3A, the fasteners 308 fit
10 through a set of holes 12 for a designated location on the bench
11 top 11, and are coupled to the receiving wells 307 for fastening
12 the tile 301 to the top surface of the bench top 11.
13

14 In a preferred embodiment, the fasteners 308 comprise
15 screws, but those skilled in the art will recognize, after
16 perusal of this application, that other types of fasteners would
17 also be workable with the devices and substances described
18 herein, and are within the scope and spirit of the invention.
19

20 The top face 302 of the tile 301 comprises a set of
21 receiving areas 309 for insertion of a corresponding set of
22 standardized packages 401. The top face 302 also comprises a set
23 of one or more top indentations 310 and top ribs 311. A set of
24 holes 312 are disposed in at least some of the top indentations
25 310, so that liquids in those top indentations 310 may drain.
26 Each receiving area 309 comprises a depression 320, into which a
27 package 401 (figure 3B) may be placed.
28

1 Each depression 320 comprises a pair of side walls 321
2 disposed parallel to each other, a pair of intermediate barriers
3 322 disposed so as to divide the depression 320 into a set of
4 three subdepressions 323, each intermediate barrier 322 having a
5 pair of stubs 324. Each pair of stubs 324 is aligned with each
6 other and disposed parallel to the side walls 321, so that a
7 package 401 may be snugly fitted into one of the three
8 subdepressions 323.

9
10 Each stub 324 comprises a first and second stub side
11 325 and a stub end 326. The stub sides 325 for the stub 324 are
12 disposed parallel to the stub sides 325 of the matching stub 324,
13 and parallel to the side walls 321. The stub end 326 for the
14 stub 324 is generally disposed so that the stub 324 is relatively
15 short compared with the package 401.

16
17 When a package 401 is fitted into a side one of the
18 three subdepressions 323, it is disposed with a first package
19 side 402 (figure 3B) disposed next to a first side wall 321 and
20 with a second package side 402 disposed next to one of the stubs
21 323, in particular, next to one of the stub sides 324. A first
22 end of the second package side 402 is disposed next to a first
23 stub 323, while a second end of the second package side 402 is
24 disposed next to a second stub 323, the second stub 323 being the
25 matching stub 323 aligned with the first stub 323.

26
27 Alternatively, a package 401 may be fitted into a
28 center one of the three subdepressions 324. In this case, it is

1 disposed with a first package side 402 disposed next to a first
2 pair of stubs 323, and a second package side 402 next to a second
3 pair of stubs 323. A first end 403 (figure 3B) of the second
4 package side 402 is disposed next to a first stub 323 in its
5 pair, while a second end 403 of the second package side 402 is
6 disposed next to a second stub 323 in its pair, the second stub
7 323 being the matching stub 323 aligned with the first stub 323.

8
9 Each subdepression 323 comprises a pair of receiving
10 holes 325 for insertion of a corresponding lever 404 (figure 3B)
11 and a corresponding spring lock 405 (figure 3B) of the package
12 401 to be disposed in the subdepression 323. When the package
13 401 is fitted into the subdepression 323, the lever 404 of the
14 package 401 is disposed in a first one of the receiving holes
15 325, and the spring lock 405 of the package 401 is disposed in
16 the second one of the receiving holes 325.

17
18 Figure 3B (comprising 6 parts, individually figures 3B-
19 1, 3B-2, 3B-3, 3B-4, 3B-5, and 3B-6) shows a standardized package
20 for coupling to the tile.

21
22 In a preferred embodiment, a standardized package 401
23 comprises a molded plastic tray 406 and a thin cover 407 affixed
24 to the tray 406, such as by a heat weld, a glue, or other known
25 means. In a preferred embodiment, the thin cover 407 may
26 comprise a plastic or metallic sheet 408, laminated on an outside
27 side 409 with plastic and printed thereon with identifying
28 information, and coated along an edge area 410 on an inside side

1 411 with a fixative 412 and affixed by means of that edge area
2 410 to a corresponding tray surface 413.

3
4 In a preferred embodiment, the fixative 412 comprises a
5 heat weld, but those skilled in the art will recognize, after
6 perusal of this application, that other types of bonding
7 techniques would also be workable, such as crimping or welding,
8 or glue, and are within the scope and spirit of the invention.

9
10 The tray 406 comprises a tray frame 420, having a
11 rectilinear shape with a top surface 421. The top surface
12 includes the tray surface 413 for bonding with the cover 407, and
13 also includes a handle region 422 with a hole 423 disposed
14 therein.

15
16 The cover 407 also comprises a cover lip 414 disposed
17 on at least one end of the package 401, having a sufficient size
18 to be grasped by an operator and removed from the tray 406.

19
20 The tray frame 420 comprises a pair of side surfaces
21 424, disposed perpendicular to the top surface 421. The side
22 surfaces 424 form the package sides 402 and the ends 403 of the
23 packet sides 402.

24
25 The tray frame 420 comprises a first end surface 425,
26 disposed perpendicular to the top surface 421 and to the side
27 surfaces 424, and forming a box shape underneath the handle
28

1 region 422 and the hole 423, providing additional sturdiness in
2 that region.

3
4 The tray frame 420 comprises a second end surface 426,
5 disposed perpendicular to the top surface 421 and to the side
6 surfaces 424, and having the spring lock 405 disposed thereon.

7
8 The tray frame 420 comprises a set of tray ribs 427,
9 disposed underneath the top surface 421 and near the side
10 surfaces 424, providing additional sturdiness to the tray 406 and
11 the side surfaces 424.

12
13 The tray frame 420 is coupled to a well frame 440,
14 which comprises a rectilinear shape having a pair of well sides
15 441, a well bottom 442, a set of wells 460, a first well end 443
16 near the first end surface 425, and a second well end 444 near
17 the second end surface 426.

18
19 The wells 460 each comprises a truncated wedge shape,
20 having a single well bottom 461 that is U-shaped, with the plane
21 of the U-shape parallel to the side surfaces 424, and a pair of
22 single well sides 462 that are flat and each have a trapezoidal
23 shape. Each single well bottom 461 comprises a set of three
24 relatively straight surfaces, a well horizontal bottom 463 that
25 is relatively flat and horizontal (and may comprise a V shape
26 with a arms of the V shape disposed about 2.5 degrees from
27 horizontal), and a pair of well semibottoms 464 that are flat and
28 disposed at an angle of about 9.5 degrees from the vertical.

1 The single well bottoms 461 are disposed in a
2 continuous sequence so as to merge to form the well bottom 442.
3 The well bottom 442 is therefore formed without seams and with
4 ridges 465 formed by well semibottoms 464 adjacent to each other.

5
6 The single well sides 462 are disposed in a continuous
7 sequence so as to merge to form the well sides 441. The well
8 sides are therefore formed without seams and without ridges.

9
10 Each well 460 is formed with a molded label 466 that is
11 unique within the package 410. In a preferred embodiment, the
12 labels 466 are formed by molding the plastic of the tray 406, but
13 those skilled in the art will recognize, after perusal of this
14 application, that the labels could be workably formed by
15 alternative means, such as etching, printing, or scoring, and
16 that such alternative means are within the scope and spirit of
17 the invention. In a preferred embodiment, the labels 466 may
18 each comprise a single digit "0", "1", "2", "3", "4", "5", "6",
19 "7", "8", or "9". Alternatively, the number "10" may be
20 substituted for the digit "0".

21
22 A first well 460 with a label 466 of "0" is disposed
23 near the first end surface 425 and has the lever 404 disposed
24 thereon.

25
26 A second well 460 with a label 466 of "1" is disposed
27 near the second end surface 426 and has a set of end ribs 467
28 disposed thereon.

1 The lever 404 comprises a right-angled lever lip 480,
2 having a first lever surface 481 and a second lever surface 482,
3 supported by a set of lever ribs 483 disposed between the first
4 lever surface 481 and the first well 460 and underneath the
5 second lever surface 482. The lever lip 480 is disposed at
6 parallel to the first end surface 425 and sized to fit into the
7 corresponding receiving hole 325. In a preferred embodiment, the
8 first lever surface 481 has at least one lip hole 484 disposed
9 thereon, to promote mating at a surface of the tile 301 near the
10 receiving hole 325.

11
12 The spring lock 405 comprises a right-angled spring lip
13 500, having a first spring surface 501 and a second spring
14 surface 502, supported by a set of first spring ribs 503
15 underneath the second spring surface 502. The first spring
16 surface 501 comprises a section of the second end surface 426
17 having a pair of cuts 504 disposed thereon, a reinforced spring
18 base 505 disposed at a base of the pair of cuts 504, and a pair
19 of second spring ribs 506 disposed underneath the second spring
20 surface 426 near the cuts 504. The spring lip 500 is disposed in
21 parallel to the second end surface 426 and sized to fit into the
22 corresponding receiving hole 325.

23
24 An inside surface 520 of the tray 406 comprises a set
25 of inside wells 521 corresponding to the wells 460. Each
26 adjacent pair of inside wells 521 is separated by a well divider
27 522. Each well divider 522 comprises a U-shaped, with the plane
28 of the U-shape perpendicular to the side surfaces 424, and having

1 a taper from thicker near a bottom end 523 disposed near the
2 bottom 524 of the inside wells 521 to thinner near a top end 525
3 disposed farther from the bottom 524 of the inside wells 521.

4
5 Each well divider 522 comprises a center 526, at a
6 bottom curve of the U-shape, that has an indentation 527, thus
7 forming two lips 528 disposed between each adjacent pair of
8 inside wells 521.

9
10 Each well divider 522 comprises a well top 527, at a
11 pair of top ends 528 of the U-shape, disposed with a gap 529
12 between the well top 527 and the cover 407.

13
14 In a preferred embodiment, the well dividers 522 are
15 sized so that each inside well 521 may hold 750 microliters ($3/4$
16 of a milliliter) of liquid without spilling over to an adjacent
17 inside well 521. However, if the amount of liquid in an inside
18 well 521 exceeds 750 microliters, the liquid will spill over the
19 bottom curve of the U-shape of the well divider 522, and thus
20 spill into the adjacent inside well 521.

21
22 In a preferred embodiment, the robotic device 10
23 operates by orienting a slide 540 with a specimen 541 vertically
24 for insertion into the inside well 521, i.e., with the flat
25 surfaces of the slide 540 being perpendicular to a plane of the
26 ground. When the slide 540 is inserted into the inside well 521,
27 a liquid content 542 of the inside well 521 will coat the
28 specimen 541 by means of capillary action.

1 This capillary action is particularly promoted if the
2 slide 540 is coupled to a second slide 540 to form a slide pair
3 543, with the specimen 542 sandwiched between the slide 540 and
4 the second slide 540 of the slide pair 543, and with the slide
5 540 and the second slide 540 maintained a selected separation
6 distance apart of preferably about 146 microns +/- 12 microns.
7 However, those skilled in the art will recognize, after perusal
8 of this application, that slides of differing sizes and selected
9 separation distances would be workable, and are within the scope
10 and spirit of the invention. For example, a selected separation
11 distance for a slide 540 or a slide pair 543 for frozen tissue
12 may comprise a substantially larger size, such as about 200
13 microns. A preferred embodiment of the slide pair 543 is shown
14 in one or more of the following U.S. Patents, hereby incorporated
15 by reference as if fully set forth herein: 4,731,335; 4,777,020;
16 4,798,706; 4,801,431; 4,975,250; 5,002,736; 5,023,187; and
17 5,116,727, and may be used in conjunction with inventions
18 therein.

19
20 It has been found by the inventors that the selection
21 of the particular volume, 750 microliters, for each inside well
22 521 is particularly advantageous. This selected volume of liquid
23 is generally sufficient to perform all the steps of typical
24 immunohistochemical stains and other assay protocols (generally,
25 with this selected volume of liquid, slides 540 or slide pairs
26 543 may be inserted into the inside well up to about three
27 times). However, this selected volume of liquid is not so large
28 that nonspecimen parts of slides 540 or slide pairs 543 (such as

1 the back or sides) are regularly excessively contaminated. This
2 selected volume of liquid also has the advantage, particularly
3 when held in an inside well 521 having a single well bottom 461
4 with relatively steep sides (formed by the well horizontal bottom
5 463 and the well semibottoms 464), that there is a reduced
6 surface/volume ratio. This provides for lesser evaporation of
7 the liquid in the inside well 521.

8
9 It has also been found by the inventors that the
10 selected shape of the inside well 521 is particularly
11 advantageous. This particular shape promotes self-levelling and
12 reduced evaporation, as noted herein. Moreover, this particular
13 shape promotes centering within the inside well 521 of small
14 amounts of liquid (about 150 microliters), due to surface tension
15 repulsion of the liquid by the well semibottoms 464. Centering
16 of the liquid promotes capillary action when a slide 540 or slide
17 pair 543 is inserted into the inside well 521.

18
19 Preferred filling amounts for content of the inside
20 well 521 are about 350 microliters when the compound or mixture
21 is not too expensive, and about 200 microliters when the compound
22 or mixture is relatively expensive (or when other reasons exist
23 to restrict the amount, such as the compound or mixture being
24 dangerous in quantity).

25
26 Preferred dimensions and tolerances for tiles 301 and
27 packages 401 are shown in figures 3A and 3B.

28

1 Figure 3C (comprising 2 parts, individually figures 3C-
2 1 and 3C-2, and multiple page figure 3C-3) shows first and second
3 standardized slide carriers for coupling slides to a compound or
4 mixture in a package.

5
6 In a preferred embodiment, a first standardized slide
7 carrier 560 comprises a frame 561, a coupling ring 562, a set of
8 slide frames 563, and a set of feet 564. The frame 561 comprises
9 a metal frame comprising a set of four horizontal elements (a top
10 565, a slide top 566, a slide bottom 567, and a bottom 568), and
11 a set of four support posts 569. The top 565, slide top 566,
12 slide bottom 567, and bottom 568 are coupled and supported by the
13 four support posts 569, to make the frame 561 rigid and sturdy.

14
15 The coupling ring 562 is coupled to the top 565 by
16 means of a pair of ring supports 570, that connect the coupling
17 ring 562 to the rest of the top 565. The coupling ring 562 is a
18 roughly circular element and has a similarly shaped ring base 571
19 underlying it and coupled to it by means of screws 572 disposed
20 through the ring supports 570 with their axes aligned vertically.
21 The coupling ring 562 also has a ring bumper 573 disposed on top
22 and coupled to it by means of glue or another fastening
23 technique.

24
25 The coupling ring 562 comprises a plastic disk 574,
26 defining a circular hole 575 (smaller to and aligned with a
27 circular hole 576 defined by each of the coupling ring 562, the
28 ring base 571, and the ring bumper 573), and having a circular

1 raised lip 577 surrounding the hole 576. The disk 574 also
2 comprises a circular flat portion 578 disposed between the
3 coupling ring 562 and the ring base 571, sufficiently large so
4 that the disk 574 cannot fall out from between the two. The
5 coupling ring 562 is thus disposed and shaped so the robot's
6 rubber securing ring 23b may couple thereto and form a firm (but
7 easily detachable) coupling.

8
9 If the robot's rubber securing ring 23b is slightly
10 misaligned from the disk 574 in the X or Y direction or both, the
11 disk 574 will realign within the rubber securing ring 23b by
12 sliding within the region defined between the coupling ring 562
13 and the ring base 571. The rubber securing ring 23b and the disk
14 574 may thus couple anyway despite slight misalignment in the X
15 or Y direction or both, up to about 2 mm in a preferred
16 embodiment. Similarly, if the robot's rubber securing ring 23b
17 is slightly misaligned from the disk 574 in the Z direction, an
18 outside part of the rubber securing ring 23b will bump against
19 the ring bumper 573, so the rubber securing ring 23b and the disk
20 574 may thus couple anyway despite slight misalignment in the Z
21 direction, up to about 2 mm in a preferred embodiment.

22
23 The slide frames 563 (preferably there are three of
24 them) are coupled to the slide top 566, by means of a set of
25 screws 580 disposed with their axes aligned vertically. Each
26 slide frame 563 comprises a set of slide positions 581 for
27 holding standardized slides 540 or slide pairs 543. The slide
28 bottom 567 is disposed to support the slide frames 563 relatively

1 tightly. An underside 582 of the slide bottom 567 is labelled
2 with a set of letters 583 "A", "B", and "C", disposed with one
3 letter near each slide frame 563, and a set of digits 584 "1",
4 "2", "3", "4", "5", "6", "7", "8", "9", and "0", disposed with
5 one digit near each slide position 581 in each slide frame 563.
6 A preferred embodiment for the slide frame 563, and related
7 inventions, are shown in one or more of the following U.S.
8 Patents, hereby incorporated by reference as if fully set forth
9 herein: 4,731,335; 4,777,020; 4,798,706 4,801,431; 4,975,250;
10 5,002,736; 5,023,187; and 5,116,727, and may be used in
11 conjunction with inventions shown therein.

12
13 The set of feet 564 (preferably there are four of them)
14 are coupled to the frame bottom 568, by means of being
15 integrately formed therewith. The feet 564 each comprise a
16 wedge-shaped element 590, with a relatively thicker top end 591
17 and a relatively thinner bottom end 592, shaped and sized to fit
18 into the top indentations 310 in the top face 302 of the tile 301
19 with a bit of extra space.

20
21 If, when the robot hand 23 deposits the slide carrier
22 560 onto the tile, the slide carrier's feet 564 are slightly
23 misaligned from the tile's top indentations 310 in the X or Y
24 direction or both, the wedge-shaped element 590 will realign
25 within the top indentations 310 by force of the weight of the
26 slide carrier 560, so the slide carrier's feet 564 and the top
27 indentations 310 may thus couple anyway despite slight
28 misalignment in the Z direction, up to about 2 mm in a preferred

1 embodiment. Similarly, if the slide carrier's feet 564 are
2 slightly misaligned from the top indentations 310 in the Z
3 direction, the slide carrier 560 will fall into the top
4 indentations 310, so the slide carrier's feet 564 and the top
5 indentations 3120 may thus couple anyway despite slight
6 misalignment in the Z direction, up to about 2 mm in a preferred
7 embodiment.

8
9 In a preferred embodiment, a second standardized slide
10 carrier 600 also comprises a frame 601, a coupling ring 602, a
11 slide frame 603, and a set of feet 604. The second standardized
12 slide carrier 600 comprises a similar structure to the first
13 standardized slide carrier 560.

14
15 The first standardized slide carrier 560 comprises a
16 generally cubic shape and is adapted for holding a set of three
17 slide frames 563, each with 10 slide pairs (i.e., a total of 60
18 slides). However, the second standardized slide carrier 600
19 comprises a rectilinear shape and is adapted for holding a slide
20 frame 603 with 10 slide pairs (i.e., 20 slides).

21
22 The first standardized slide carrier 560 comprises a
23 roughly circular coupling ring 562, coupled to the top 565 by
24 means of a pair of ring supports 570, which has a similarly
25 shaped ring base 571 underlying it, and which also has a ring
26 bumper 573 disposed on top. However, the second standardized
27 slide carrier 600 comprises a coupling ring 602 that is
28 integrated into the rest of a top 605 and is thus rectilinear,

1 which has a similarly shaped ring base 606 underlying it, and
2 which also has a ring bumper 607 disposed on its top. The ring
3 bumper 607 is roughly circular but shaped to match the shape of
4 the second standardized slide carrier 600.

5
6 The first standardized slide carrier 560 preferably
7 comprises a set of three slide frames 563. However, the second
8 standardized slide carrier 600 preferably comprises a single
9 slide frame 608 having a plurality of slide positions 609. The
10 underside 610 of the slide frame 608 is not labelled; rather, a
11 pair of sides 611 of the slide frame 608 are labelled with a set
12 of integers 612 "1", "2", "3", "4", "5", "6", "7", "8", "9", and
13 "10", disposed with one digit near each slide position 609 in the
14 slide frame 608.

15
16 The first standardized slide carrier 560 preferably
17 comprises a set of four feet 564. However, the second
18 standardized slide carrier 600 preferably comprises a set of only
19 two feet 613.

20
21 Multiple page figure 3C-3, comprising 13 pages, shows
22 detailed parts drawings for the first standardized slide carrier
23 560 and the second standardized slide carrier 600.

24 25 WORKSTATION DEVICES

26
27 In addition to packages 401, the tile 301 at a
28 workstation 13 may be coupled to another type of device for

1 operating on samples, whether carried by slides 540, slide pairs
2 543, or another carrying medium such as a beaker, test tube or
3 wafer. In a preferred embodiment, the tile 301 at a workstation
4 13 may be coupled to one or more of the following devices:

5

6 The workstation 13 may comprise a centrifuge, a
7 diffusion device, a distillation device, or other separation
8 device.

9

10 The workstation 13 may comprise a DNA crosslinking
11 device.

12

13 The workstation 13 may comprise an electroporator.

14

15 The workstation 13 may comprise a laser device or other
16 optical device.

17

18 The workstation 13 may comprise a microwave device, a
19 shielded radioactive sample, or other radiation source, such as a
20 source of electromagnetic or ionic radiation.

21

22 The workstation 13 may comprise an incubation oven or
23 other heating unit.

24

25 The workstation 13 may comprise a refrigeration element
26 or other cooling unit.

27

28

Figure 3D (comprising 2 parts, individually figures 3D-1 and 3D-2) shows a workstation having an incubation oven and a carrying medium for inserting slides 540 or slide pairs 543.

In a preferred embodiment, an incubation oven 620 comprises a chassis 621, an incubation chamber 622 a set of heat exchanger fins 623, a hydration fluid supply 624, an internal cooling element 625, a fill/drain control 626, a fluid waste receiver 627, a receiving element 628 for a carrying medium 630, and a set of heat fins 629.

The incubation chamber 622 is supported by the chassis 621 and comprises a set of chamber walls 631 disposed in a generally rectilinear form 632 with a set of rounded corners 633 to form a first part of a sealed fluid-tight box 634 when the carrying medium 630 is disposed for operation. When the carrying medium 630 is disposed for operation, the slides 540 or slide pairs 543 in the carrying medium 630 may be heated with moist heat formed by heating the incubation chamber 622 while disposing a hydrating fluid therein, and thus incubated. Incubation of slides 540 or slide pairs 543 is known in the art.

The heat exchanger fins 623 are disposed in the incubation chamber 622 in an array. The array is disposed to match, but not contact, a set of slides 540 or slide pairs 543 disposed in the carrying medium 630. There should be one of the heat exchanger fins 623 for each slide 540 or slide pair 543, or at the least, for each pair of slides 540 or slide pairs 543.

1 Each one of the heat exchanger fins 623 has a height sufficient
2 to heat the entire slide 540 or slide pair 543, or at least a
3 portion of the slide 540 or slide pair 543 to include the sample.
4

5 A horizontal plate isolates the heat exchanger fins 623
6 from the hydration fluid supply 624. The heat exchanger fins 623
7 may each comprise a resistive element such as a metallic wire,
8 coupled to a voltage source 634 disposed outside the incubation
9 chamber 622. The voltage source 634 is coupled to a voltage
10 regulator 635 to regulate the temperature of the incubation
11 chamber 622, and thus of the slides 540 or slide pairs 543, to a
12 selected temperature in steps of 1 degree Celsius between ambient
13 temperature to about 100 degrees Celsius. Heating elements and
14 regulators are known in the art.
15

16 The incubation oven 620 is triggered when first coupled
17 to the robotic system, and controlled to a temperature selected
18 by the control station 14. Typically, the control station 14
19 will set the regulated temperature of the incubation oven 620 to
20 a room temperature such as 25 degrees Celsius, will set the
21 regulated temperature of the incubation oven 620 to an operating
22 temperature such as 95 degrees Celsius a few minutes before the
23 incubation oven 620 is to be used in a process step, and will set
24 the regulated temperature of the incubation oven 620 to a room
25 temperature or to a second operating temperature such as 37
26 degrees Celsius after the incubation oven 620 is used in a
27 process step and before it is to be used in a second process
28

1 step. Each process step designating the incubation oven 620
2 indicates an operating temperature for that process step.
3

4 The hydration fluid supply 624 comprises a source, such
5 as a bottle, into which a hydrating fluid 636 is placed and from
6 which hydrating fluid 636 is drawn during operation of the
7 incubation oven 620, and a fluid well 637 in which a selected
8 level of hydrating fluid 636 is maintained. The selected level
9 of hydrating fluid 636 is maintained by means of an automatic
10 replenisher having a combination of a reservoir and valve,
11 disposed to maintain a constant level of hydrating fluid 636 in
12 the fluid well 637 available for evaporation into the incubation
13 chamber 622, similar to a bird feeder. The fill/drain control
14 626 provides for filling and draining the hydrating fluid 636
15 from the fluid well 637. Flow regulation and fluid level
16 regulation are known in the art.
17

18 The selected level of hydrating fluid 636 may be
19 adjusted to account for differing assay protocols. For example,
20 an assay protocol for hybridization may generally require heating
21 and cooling without drying out the sample. Alternatively, other
22 assay protocols, such as those for heating a xylene mixture, may
23 require a relatively dry heat.
24

25 In a preferred embodiment, the hydrating fluid 636 may
26 comprise (per 10 liters) 9980 milliliters nanopure water, 20
27 milliliters Tween-20, and 10 grams sorbic acid. However, those
28 skilled in the art would recognize, after perusal of this

1 application that plain water, a known buffer solution, or another
2 substance for incubation of tissue, would also be workable for
3 the hydrating fluid 636, and that such substances would be within
4 the scope and spirit of the invention.

5
6 The internal cooling element 625 is disposed in the
7 chassis 621 near the incubation chamber 622 to cool the
8 incubation oven 620 and those of its elements that do not need to
9 have an raised temperature. The internal cooling element 625
10 comprises a fan 638 coupled to the voltage source 634 and to a
11 temperature regulator 639, such as a thermostat, to maintain the
12 chassis 621 at a selected temperature. The heat fins 629 also
13 serve to aid in regulating the incubation chamber 622 to a
14 selected temperature. Temperature regulation is known in the
15 art.

16
17 The fluid waste receiver 627 comprises a chamber for
18 receiving excess hydrating fluid 636 not evaporated by the heat
19 exchanger fins 623, and other fluids that may be condensed by the
20 internal cooling element 625. The fluid waste receiver 627 may
21 be detachable for emptying.

22
23 The receiving element 628 comprises a set of receiving
24 slots 640 molded into a bottom 641 of the incubation chamber 622,
25 disposed to receive a set of feet 641 of the carrying medium 630.
26 The carrying medium's feet 641 are similar to those of the first
27 standardized slide carrier 560 or the second standardized slide
28

1 carrier 600, so the receiving element 628 is similar to the top
2 indentations 310 of the tile 301.

3

4 The carrying medium 630 for inserting slides 540 or
5 slide pairs 543 into the incubation oven 620 is similar to the
6 first standardized slide carrier 560, and comprises a frame 651,
7 a coupling ring 652, a set of slide frames 653, and a set of feet
8 654. It further comprises a slide holder cover 655, a set of
9 ventilation openings 656, and a cover latch 657.

10

11 The frame 651 is similar to the first standardized
12 slide carrier's frame 561, and comprises a metal frame comprising
13 a set of four horizontal elements (a top 658, a slide top 659, a
14 slide bottom 660, and a bottom 661), and a set of four support
15 posts 662. Rather than being flat as in the first standardized
16 slide carrier's frame 561, the bottom 661 comprises a V shape
17 with the bottom of the V shape in the center, to carry
18 condensation away from the slides 540 or slide pairs 543. Other
19 frame elements may also be bent at angles or into V shapes to
20 direct condensation away from the slides 540 or slide pairs 543.

21

22 The slide holder cover 655 is disposed over the frame
23 651, and comprises a solid shell of a lightweight material such
24 as a rigid plastic. The slide holder cover 655 comprises a set
25 of four shell sides 662, a set of downward sloping corners 663,
26 and a rounded topmost part 664, with the set of ventilation
27 openings 656 defined by gaps in the topmost part 664.

28

1 The ventilation openings 656 comprise a set of openings
2 665 with a slidable disk 666 disposed around the coupling ring
3 652 (and related assembly) similar to the first standardized
4 slide carrier's coupling ring 562 (and related assembly, such as
5 the ring base 571, ring bumper 573, plastic disk 574, circular
6 hole 575, circular hole 576, circular raised lip 577, and
7 circular flat portion 578). The slidable disk 666 defines a set
8 of slidable openings 667 generally corresponding to the
9 ventilation openings 656, a set of slidable masks 668 also
10 generally corresponding to the ventilation openings 656, and a
11 lip 669 for sliding the slidable disk 666 to adjust the
12 ventilation openings 656 by alternatively uncovering them with
13 the slidable openings 667 or covering them with the slidable
14 masks 668.

15
16 The slide holder cover 655 and the ventilation openings
17 656 are preferably shaped (as shown in figure 3D) to optimize
18 effects of condensation of the hydrating fluid 636 and carry
19 condensate away from the slides 540 or slide pairs 543. In
20 particular, the slide holder cover 655 and the ventilation
21 openings 656 are preferably trapezoidally shaped to cause the
22 hydrating fluid 636 to condense and drip back into the incubating
23 chamber 622, rather than evaporate into the local atmosphere.

24
25 The cover latch 657 comprises a V-shaped element 669
26 coupled to one of the shell sides 662, and a peg 670 coupled to
27 the slide top 659. The V-shaped element 669 is disposed to just
28

1 fit over the peg 670, so that a reasonably firm, but still easily
2 removable, latch is made.

3

4 In a preferred embodiment, the incubation oven 620 is
5 prepared with the following steps:

6

7 1. The operator fills the hydration fluid supply 624
8 and, if necessary, empties the fluid waste receiver 627.

9

10 2. The operator adjusts the fill/drain control 626 to
11 regulate the level of hydrating fluid 636 to a selected level.

12

13 3. The operator prepares the slides 540 or slide
14 pairs 543 according to a desired assay protocol, and configures
15 the robotic system to perform the program for that assay
16 protocol.

17

18 4. The operator inserts the slides 540 or slide pairs
19 543 into the carrying medium 630 by means of the slide holder
20 cover 655, and replaces the slide holder cover 655 on the
21 carrying medium 630. The operator sets the ventilation openings
22 656 to adjust for ambient humidity levels. Preferably, the
23 ventilation openings 656 should be as wide open as possible while
24 at the same time allowing the chemistry in the capillary gap of
25 the slide pair 543 to maintain a level above 75% of capillary gap
26 for an entire hybridization process step.

27

28

1 5. The operator places the slide carrying medium 630
2 in a HOME position tile 301 and directs the control station 14 to
3 initiate the assay protocol.

4
5 The incubation oven 620 may be used in conjunction with
6 inventions disclosed in one or more of the following U.S.
7 Patents, hereby incorporated by reference as if fully set forth
8 herein: 4,731,335; 4,777,020; 4,798,706; 4,801,431; 4,975,250;
9 5,002,736; 5,023,187; and 5,116,727.

10
11 In a preferred embodiment, where the workstation 13
12 comprises a device that should be engaged to operate on the
13 sample, coupling the carrying medium to the device requires two
14 steps: (1) The carrying medium is first coupled to or inserted
15 into the device. (2) The device is triggered.

16
17 As with the incubation oven 620, the device may be
18 triggered when first coupled to the system, and controlled by the
19 control station 14. Alternatively, the device may be triggered
20 by a switch (triggered by contact with the robotic arm), or
21 preferably, by contact with the carrying medium by means of a
22 contact switch, proximity switch, or a weight-triggered switch
23 that detects the presence of the carrying medium or its having
24 been coupled to the device.

25
26 / / /
27
28

1 OPERATION OF THE PACKAGE IN THE ROBOTIC SYSTEM
2

3 Figure 3E is a flowchart of a preferred method of
4 operating the robotic system with standardized packages and
5 contents.
6

7 In a preferred embodiment, at a step 681, the tray 406
8 is filled with contents 542 comprising a selected amount of a
9 selected reagent, other bioactive or chemoactive compound or
10 mixture, or buffer.
11

12 At a step 682, the tray 406 has the cover 407 sealed
13 thereon.
14

15 At a step 683, the tray 406, contents 542, and cover
16 407, are transported to a location having the robotic device 10.
17 The configuration of the well dividers 522 permits the liquid
18 contents to flow easily between the inside wells 521 during
19 shipment and prior to placement in a tile 301.
20

21 In a preferred embodiment, the contents 542 of the tray
22 406 comprise one of a set of standardized selected reagents,
23 other bioactive or chemoactive compounds or mixtures, or buffers,
24 known to programmers of the robotic device 10. Because the
25 contents 542 are standardized and known to programmers of the
26 robotic device 10, an assay protocol may be preprogrammed and
27 preloaded into the robotic device 10, for dynamic selection by an
28 operator.

1 At a step 684, an operator of the robotic device 10
2 places a plurality of tiles 301 in the robotic device 10, and
3 affixes those tiles 301 to the robotic device 10 with screws or
4 other affixing objects.

5
6 At a step 685, the operator places one or more trays
7 406, each with its cover 407 still sealed, in a set of selected
8 tiles 301.

9
10 At a step 686, the operator removes the covers 407 from
11 the trays 406, instructs the robotic device 10 as to the location
12 of each such tray 406 and its contents 542, and commands the
13 robotic device 10 to begin one or more preprogrammed assay
14 protocols. As described herein, the preprogrammed assay
15 protocols may be one or more assay protocols with which the
16 robotic device 10 is started, or may be one or more assay
17 protocols that are added to an already ongoing set of assay
18 protocols.

19
20 In a preferred embodiment, the strength of the fixative
21 that affixes the cover 407 to the tray 406 exceeds any likely
22 force for removal that might occur during shipment, but is less
23 than a force for removal required for overcoming the spring lock
24 405. The operator may therefore remove the cover 407 from the
25 tray 406 while the tray 406 is locked into the tile 301 by means
26 of the lever 404 and the spring lock 405, without the tray 406
27 coming undone from the tile 301 due to the force of removal.

28

1 In a preferred embodiment, the robotic device 10
2 comprises a memory with a set of preprogrammed assay protocols,
3 that have been previously programmed and loaded into memory, and
4 that are selectable by a set of assay protocol names. The
5 operator may therefore select an assay protocol by name at the
6 time it is desired to conduct the assay, without having to
7 reprogram the robotic device 10 each time it is desired to
8 conduct that assay. In a preferred embodiment, a set of
9 preprogrammed assay protocols are previously programmed,
10 transferred to an intermediate storage medium such as a diskette,
11 tape, or network, and loaded into the memory of the robotic
12 device 10 by means of a operator command. The operator command
13 to load the preprogrammed protocol may also be subject to
14 security confirmation.

15
16 The standardized contents 542 of the trays 406 may
17 comprise a set of alcohols.

18
19 The standardized contents 542 of the trays 406 may
20 comprise a set of antibodies.

21
22 The standardized contents 542 of the trays 406 may
23 comprise a set of blocking agents, such as hydrogen peroxide
24 block or a serum block.

25
26 The standardized contents 542 of the trays 406 may
27 comprise a set of buffer solutions, preferably a phosphate
28 buffered saline with a pH of about 7.2. In a preferred

1 embodiment, buffer solutions should include a surfactant for best
2 operation with the capillary gap of the slide pair 542. The
3 surfactant is bridge or preferably tween (the latter available
4 from Fisher Scientific Co.), optimized for use with the capillary
5 gap in a slide pair 543 with about a 1% to 2% solution of tween
6 in water.

7
8 The standardized contents 542 of the trays 406 may
9 comprise a set of chromagens, including those that relate to the
10 visible range or another range of the electromagnetic spectrum
11 (such as infrared or ultraviolet).

12
13 The standardized contents 542 of the trays 406 may
14 comprise a set of DNA probes.

15
16 The standardized contents 542 of the trays 406 may
17 comprise a set of enzymes.

18
19 The standardized contents 542 of the trays 406 may
20 comprise a set of fixatives.

21
22 The standardized contents 542 of the trays 406 may
23 comprise a set of linking molecules, such as avidin biotin
24 conjugate.

25
26 The standardized contents 542 of the trays 406 may
27 comprise a set of staining agents, such as hematoxylin stain or
28 eosin stain.

1 The standardized contents 542 of the trays 406 may
2 comprise a set of washes, such as water.

3
4 A set of preferred assay protocols is described in an
5 appendix.

6 7 SYSTEM CONTROL BY OPERATOR 8

9 In order to use the system of this invention the
10 operator (which might be a human user or a control processor) may
11 first determine the processes that are to be carried out the
12 apparatus. Each step of each process may be defined. To assist
13 the user an index of work stations may be provided to allow the
14 user to determine which process steps can be employed.
15 Alternatively, each work station can be represented by an icon on
16 the CRT display and a help index made available that the user may
17 determine the capabilities of each work station by referring to
18 the icon and its associated help screen.

19
20 As previously described with reference to figures 1-2,
21 the apparatus of the invention uses a locating grid or template
22 presenting the operational work area reachable by the robotic
23 device 10 in which the work station locations may be defined.
24 Each position on the grid is accurately determined and can be
25 imparted to the computer to provide certainty of location. The
26 exact relative position of each work station may be stored in the
27 control system. The use of the predetermined grid locations
28 permits the user of this system to have the freedom of designing

1 individual templates to match the user's need and to design the
2 steps of a process to provide relative limited ability in
3 creating processes, limited only by the available work stations.
4

5 A graphic replica of the grid in which the work
6 stations located is provided on the screen of the computer, such
7 as shown in figures 6-8. Included in this graphic is the robotic
8 arm position. In order to quickly input the steps of a process
9 to the computer (1) a template builder and (2) a process builder
10 have been created to interact with graphic replica of the work
11 area. These two tools, template builder and process builder,
12 allow the user to design a new process or modify an old process,
13 easily and quickly without the need to have knowledge of computer
14 programming. Through the use of a keyboard or mouse, the two
15 builder tools are rendered interactive with the user.
16

17 A work station grid area may have holes disposed on one
18 inch centers, or any other predetermined pattern. The columns of
19 holes may be identified by letters while the rows of locating
20 holes may be identified by numbers. Thus each hole can be
21 uniquely identified by a letter-number combination.
22

23 Work station units or peripherals have been designed
24 which have elements which cooperate with the grid locating holes
25 and thus facilitate the exact location of each station. When
26 located on the grid each work station will have a unique
27 describer positively identifying its location.
28

1 Thus the user may commence operating the system by
2 viewing a graphic representation of the work area surrounded by
3 icons representing various work stations. As will be described
4 below the user can quickly design a new template if so desired.
5 Alternatively, the template may be called up from a disk by the
6 computer.

7
8 The steps of the process are communicated to the
9 computer through the use of an interactive peripheral such as a
10 mouse. The operator locates the mouse cursor on the icon
11 representing the first step of the process and drags the icon to
12 the desired location. Thus by pointing and clicking the mouse
13 the work stations necessary to accomplish the steps of the
14 process are disposed on the graphic grid. It is of course
15 desirable that the physical workstations be located on the grid
16 in the locations shown on the display. Alternatively, the
17 location of the work station can be fed into the computer in
18 other ways, such as through the keyboard or even by locating the
19 physical work station on the grid with feedback to the computer
20 identifying the work station and location.

21
22 Thus an unsophisticated user has the ability to design
23 processes quickly imparting great flexibility to this apparatus.
24 It should of course be recognized that this information can be
25 stored on a disk and the apparatus set up accomplished by reading
26 the information off a disk into the memory of the computer.

27
28

1 In creating the template the operator uses a mouse to
2 draw replicas of each station on the screen, such as shown in
3 figure 7, a template building screen. Each station is given a
4 unique identification which may be a name, symbol or code. The
5 dimensions of the station may be drawn on the screen and in
6 particular it is essential that the height of the work station is
7 recorded. The position, identification, height and other
8 dimensional criteria are stored in the RAM memory of the computer
9 CPU. When the template is completed it may be stored to disk as
10 a template file, to be recalled as needed.

11
12 As is not unusual in the operation of computers,
13 provisions are made to add, delete, move, resize or duplicate any
14 of the stations. Any available template previously stored may be
15 recalled to be used or to assist in the creation of new
16 templates. Of course the apparatus may have the ability to
17 enable the operator to print out a graphic replica of the screen
18 and a list of station positions, identifications, heights or
19 other dimensions.

20
21 Once the template is complete the operator may use the
22 stations of the template to create a process, step by step.

23
24 The process builder, like the template builder, uses a
25 graphic replica of the workstation area on the computer screen,
26 such as shown in figure 8, a process building screen. One of the
27 templates previously created by the template tool builder
28 described above, is recalled from memory and displayed on the

1 screen together with the work area. The screen cursor is moved
2 to the desired station icon and the particular station is
3 selected. This procedure may utilize a mouse and a point and
4 click procedure.

5
6 Each station of the process is selected in sequence and
7 the station is then added to a list denoting the steps of the
8 process in sequential order. The robotic device would ultimately
9 be controlled to move to each of these stations in the order in
10 which they were added the process list. Since the
11 characteristics of each work station were previously stored in
12 the computer, the robotic device would be programmed for the
13 proper movement. For example, the height of each station was
14 previously stored in the memory, and if the robotic arm were to
15 traverse the area in which a high work station was located, it
16 would be instructed to elevate the hand so that any sample
17 mounted thereon would clear the high work station. It is also
18 possible to design the operational area to have clear paths or
19 lanes defining travel routes for the robotic device 10. In any
20 event, the movement of the robotic device among the workstations
21 may be designed to be free of collisions based upon recognition
22 of the entity, position and geometry of the work stations. As
23 will appreciated as the number of work stations increase the
24 amount of information that should be considered in order to avoid
25 collisions and otherwise avoid conflicts in instructions also
26 increases.

27

28

1 Following the graphic design of the steps of the
2 process, the process list would be called up on the screen and
3 the procedure for each step would be imparted, such as shown in
4 figure 9. This procedure would essentially indicate a range of
5 time each sample should remain at each station. For each step a
6 minimum time and a maximum time for the sample to remain at the
7 work station would be recorded. As noted herein, the minimum
8 time may be specified to be zero, and the maximum time may be
9 specified to be infinity. The times for each station, except
10 where the timing is critical, would allow the system a timing
11 window which can be used to avoid timing conflicts between
12 different steps of separate tasks and thus maximize the
13 multitasking capabilities of the apparatus.

14

15 PSEUDOCODE FOR DESIGNING OR RUNNING NEW PROCESSES

16

17 The method carried out by the control station 14 for
18 template building and process building may be described by
19 pseudocode shown in Tables 2-3 herein, respectively. It would be
20 clear to one of ordinary skill in the art, after perusal of the
21 specification, drawings and claims herein, that modification of
22 known processor systems to perform the functions disclosed in
23 this pseudocode (as well as in other pseudocode disclosed herein)
24 would be a straightforward task and would not require undue
25 experimentation.

26

27

28

```
1  procedure template_tool();
2
3  set up screen;
4  draw robot replica graphic;
5  draw grid;
6  display mouse cursor;
7  select template design tool;
8  while (not finished)
9      select tool;
10
11      case (edit tool)
12
13          add:      draw new station on screen via mouse by
14                    dragging mouse away from start point while
15                    having mouse button 1 depressed;
16                    update screen with a rectangle being
17                    displayed along cursor displacement;
18                    enter id via keyboard;
19                    position height of station;
20                    store position and id;
21
22          select:   move cursor to station via mouse;
23                    click mouse to select;
24                    selected station changes color to show it is
25                    selected;
26
27          delete:   click mouse button 1 to delete;
28
29          move:      place move crosshair on selected station;
30                    place cursor on crosshair;
31                    press mouse button 1 down and drag station to
32                    new position;
33                    screen update after each new grid position
34                    move;
35
36          resize:   place resize crosshair on selected
37                    station;
38                    place cursor on crosshair;
39                    press mouse button 1 down and drag station to
40                    new size;
41                    screen update after each new size;
42
43          duplicate: get current selected station position, size
44                    and height information;
45                    offset duplicate to new position;
46                    add id;
47                    store new station position and id;
```

24 After the station sequence has been entered and the
25 times for each step recorded, the process may be stored to disk
26 as a process file. The process file may be loaded in the future
27 and the apparatus used to run the same process at a later date.
28 Of course the template file may be linked to the process file so

```
1  procedure process_tool();
2
3  set up screen;
4  draw robot replica graphic;
5  draw grid;
6  draw process list;
7  display mouse cursor;
8
9      case (file tool)
10
11          get template:          display list of template files;
12                                select via mouse cursor;
13                                open selected template;
14                                display template stations on screen;
15                                hold station record in RAM;
16
17          get process:           display list of process files;
18                                select via mouse cursor;
19                                open selected process;
20                                display process list in list window;
21                                display associate template stations on
22                                the screen;
23                                hold process station records in RAM;
24
25          save process:          display list of process files;
26                                select via cursor or enter new name via
27                                keyboard;
28                                store process file to disk;
29
30      case (file tool) end;
31
32      case (select_tool):
33
34          if cursor in work station area and on a station and mouse
35          button 1 down then add station to process list;
36
37          if cursor in process list and on list member and mouse
38          button 1 down then delete from list;
39
40          case (select_tool) end;
41
42      case (window select)
43
44          Process List:          (1) set up screen;
45                                (2) display process in list mode;
46                                (3) enter min/max time via keyboard;
47                                (4) scroll down screen;
48                                (5) do steps 3-4 until finished;
49                                (6) exit back to previous window;
50
51          Run/Control:           return to Run/Control window;
52
53      end (process tool);
```

that when a process is called up from storage and run on the computer the template files used in the process may be automatically called up and displayed on the computer screen.

1 The procedure list on which the times at each step were
2 recorded may be called up at any time and for the stations still
3 not used by the robotic device, adjustments to the timing could
4 be made provided that the steps in the process which are to have
5 their timing altered have not been reached. Thus the operator
6 can adjust the timing of the steps even as the process is
7 running.

8

9

VISUAL OPERATOR INTERFACE

10

11

12

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28

Figure 6 shows a multitask monitoring screen 61 as viewed by an operator. A multitask monitoring screen 61 may be shown on a display device coupled to the computer 15, such as a display monitor. The multitask monitoring screen 61 may comprise a display section 62, a menu section 63, and a status section 64.

The display section 62 may show a representation of the robotic device 10, bench top 11, holes 12, work modules 13, and related equipment. For example, the display section 62 may show positions for workstations 13 for a selected process.

The menu section 63 may show command options and suboptions which are available to the operator and may allow the operator to select one or more command options and suboptions. For example, the menu section 63 may have a menu with the command options "GET PROCESS", "BUILD PROCESS", "PROCESS LIST", "GET TEMPLATE" and "BUILD TEMPLATE". The operator may display available command options and select one or more command options

1 in the menu section 63, by means of a pointing device, such as a
2 mouse, as is well known in the art.

3
4 The status section 64 may show a set of status
5 information about processes. For example, the status section 64
6 may show five processes which are in progress, and may show for
7 each process the current step it is on, the total time it has
8 taken (both for the current step and for the entire process), and
9 the time remaining that it will take (both for the current step
10 and for the entire process). Note that elapsed time for the
11 current step may be zero because the robotic device 11 might wait
12 for the proper time before depositing the sample in the
13 workstation 13 for that process step, e.g., holding the sample in
14 the robotic hand 23 if travel from a prior step took less time
15 than expected. The status section 64 may also show the X, Y and
16 Z position of the robotic arm.

17
18 Figure 7 shows a template building screen 71 as viewed
19 by an operator. A template building screen 71 may be shown on a
20 display device coupled to the computer 15, such as a display
21 monitor, in like manner as the multitask monitoring screen 61.
22 The template building screen 71 may comprise a display section
23 62, a menu section 63, and a status section 64, in like manner as
24 the multitask monitoring screen 61.

25
26 When using the template building tool, described
27 herein, the operator may view the template building screen 71 and
28 manipulate the commands and elements thereon by means of a

1 pointing device, such as a mouse. A detailed description of how
2 the operator may use the template builder tool is given herein.
3

4 Figure 8 shows a process building screen 81 as viewed
5 by an operator. A process building screen 81 may be shown on a
6 display device coupled to the computer 15, such as a display
7 monitor, in like manner as the multitask monitoring screen 61.
8 The process building screen 71 may comprise a display section 62,
9 a menu section 63, and a status section 64, in like manner as the
10 multitask monitoring screen 61, and a workstation section 85.
11

12 The workstation section 85 may show a set of names or
13 other identifiers of workstations 13. The operator may select
14 one or more workstations 13 for inclusion in a process, by means
15 of a pointing device, such as a mouse.
16

17 When using the process building tool, described herein,
18 the operator may view the process building screen 81 and
19 manipulate the commands and elements thereon by means of a
20 pointing device, such as a mouse. A detailed description of how
21 the operator may use the process builder tool is given herein.
22

23 Figure 9 shows a process timing screen 91 as viewed by
24 an operator. A process timing screen 91 may be shown on a
25 display device coupled to the computer 15, such as a display
26 monitor, in like manner as the multitask monitoring screen 61.
27 The process timing screen 91 may comprise a plurality of lines
28 92, each of which may have an identifier section 93, a

1 name/descriptor section 94, a minimum time section 95 and a
2 maximum time section 96.

3
4 When using the process building tool, described herein,
5 the operator may view the process timing screen 91 and enter
6 minimum times (in the minimum time section 95) and maximum times
7 (in the maximum time section 96) for each process step at each
8 line 92. Each process step may thus have a line 92 with an
9 identifier in the identifier section 93 and a name or descriptor
10 in the name/descriptor section 94.

11
12 The minimum time section 95 for a line 92 may specify a
13 minimum time which the designated process step may take, which
14 might be zero. If the minimum time is zero, additional data may
15 be noted to indicate whether the designated process step may take
16 a single tick of a timing clock for the robotic device 10, or if
17 the designated process step may be skipped entirely.

18
19 The maximum time section 96 for a line 92 may specify a
20 maximum time which the designated process step may take, which
21 might be infinity. If the maximum time is infinity, the system
22 may delay completion of the designated process step until after
23 all other process steps with finite maximum time have been
24 completed.

25
26 Each line 92 may also have an additional data section
27 97 for the designated process step, which may specify whether (1)
28 the step is to be done, (2) the step is to be skipped, or (3) the

1 process is to be "held" or temporarily halted at the designated
2 process step for input from the operator. In the latter case,
3 for example, the process might be "held" at the designated
4 process step until an operator confirms that the process should
5 continue.

6 7 MULTITASKING AND OPTIMIZATION

8
9 Having delineated all the steps of all the procedures,
10 the computer may determine the most efficient manner for carrying
11 out the procedure. The task would be simple if the steps of the
12 first process were to be completed before the apparatus started
13 on the second process. Through the use of time interleaving,
14 multiplexing or multitasking the computer is utilized to keep
15 track of multiple operations so as to perform a number of
16 different processes each having a multiplicity of steps
17 simultaneously.

18
19 In multitasking, a number of samples, each undergoing
20 separate exposures may all be worked on simultaneously. In time
21 interleaving, the robotic arm may operate through a sequence
22 which is determined by the timing of the individual steps of many
23 processes and the robotic arm transports different samples in a
24 time efficient sequence rather than a process ordered sequence.
25 Although the robotic device can only move one sample to a work
26 station at a time, the entire system is continuously monitoring,
27 scheduling and processing all tasks and their times at each
28 station concurrently. At each step the process performed at that

1 workstation continues (e.g., chemical reactions) even when the
2 robotic arm is not currently attending to it. In other words,
3 the sample is disposed in the workstation and the robotic arm
4 continues to grasp another sample. The process step continues to
5 work on the first sample while the robotic arm is attending or
6 transporting the second sample. The multiple process steps that
7 are being done, one to each sample, are being done in parallel
8 and are not serial processes.

9
10 In fact the robotic arm works on a sample for a short
11 period of time during which it usually transports a sample to a
12 work station and then leaves that sample and works on another
13 sample or samples before returning again to the first sample.
14 Thus the robotic device work on each sample is suspended during
15 the time interval that it is working on another sample or during
16 which the samples are being processed at a work station.

17
18 The multitasking of the different processes is
19 dependent upon the instructions issued to the robotic device,
20 relative to the timing of each of the steps in the multiple
21 processes and the optimization of the multitasking operations, to
22 move the samples at the scheduled times determined by the
23 computer inputs.

24
25 The computer control (software) may first determine all
26 the robotic movements necessary to complete the entire run of all
27 the steps in all the processes to be run. This determination may
28 be completed before any movement is initiated. If at any time

1 during the running of the multitasking any steps are added to one
2 or more of the processes or any of the steps are reconfigured
3 during the run, a new determination may be completed wherein the
4 computer recalculates all the movements necessary to complete the
5 run and insures that there is no time interference created by the
6 modification to the run. This method of predetermining the
7 movements can of course be replaced by a real time method of
8 determining movement but it is believed that the predetermining
9 method is more advantageous. The predetermining method
10 identifies time conflicts, if any, where the robotic device would
11 be required to perform two tasks simultaneously, resolves any
12 such conflicts that may exist, and optimizes the schedule for the
13 minimum time required to complete the entire run of the multiple
14 processes.

15
16 This method of predetermination employs certain
17 decision making procedures which are designed to permit the
18 computer to resolve time conflicts and iteratively optimize the
19 schedule. An iterative optimization method is used because the
20 complexity of scheduling different multiple tasks, each with the
21 possibility of having multiple critically timed steps, is too
22 complex to be solved by using mathematical techniques. In
23 addition, the decision making rules allow the resolution of other
24 conflicting requirements for other resources such as the
25 peripheral equipment or work station modules, which may be used
26 in conjunction with the robotic equipment.

27
28

1 As described above, a predetermined schedule may be
2 developed to resolve time and resource conflicts and the schedule
3 may be iteratively optimized to minimize the time required to
4 complete the steps of the multiple processes. In order to
5 interleave the steps of the multiple processes each step of each
6 task is examined at predetermined intervals, e.g., one minute. A
7 calculation is made of the time to completion of the current
8 step. If the step incubation time is finished a move condition
9 results. If that is the only move condition during this time,
10 i.e., only one move condition occurs, the robotic device will be
11 scheduled to move to the next step in accordance with the
12 predetermined schedule. However, if more than one sample is
13 scheduled to move time arbitration ensues. Time arbitration
14 determines the fuzzy time window for each of the time conflicting
15 steps and selects the sample in the most time critical step to
16 move. If more than one step has a critical time, the computer
17 compares the times during the previous movement and varies the
18 timing of the previous tasks to resolve or prevent bottlenecks
19 from occurring. In a similar manner a single resource can be
20 scheduled to work on two different samples during the same time
21 period and such conflicts can be resolved in a similar manner
22 using the arbitration method.

23 24 PSEUDOCODE FOR MULTITASKING

25
26 The method carried out by the control station 14 for
27 multitasking may be described by pseudocode shown in Tables 4-8
28 herein. It would be clear to one of ordinary skill in the art,

1 after perusal of the specification, drawings and claims herein;
2 that modification of known processor systems to perform the
3 functions disclosed in this pseudocode (as well as in other
4 pseudocode disclosed herein) would be a straightforward task and
5 would not require undue experimentation.
6

7 **Table 4 -- Multitasking Data Structure**

```
8  STRUCTURE TASK ARRAY [ 1500 elements ]  
9      BYTE          PROCESS NUMBER;  
10     BYTE          TASK NUMBER;  
11     CHAR [25]     TASK NAME;  
12     INTEGER       TASK X COORDINATE OF WORKSTATION;  
13     INTEGER       TASK Y COORDINATE OF WORKSTATION;  
14     LONG INTEGER  ENCODED REAL TIME FOR PICKUP OR DROPOFF;  
15     CHAR [1]      DROPOFF/PICKUP FLAG;  
  
16     CHAR [5]      MOVE_FLAG;  
17     { When TRUE the process flagged needs to move to next  
18       task in progress. This information is entered into the  
19       task array. If multiple flags are set simultaneously the  
20       process steps must be arbitrated. }  
21     CHAR [5]      RESOURCE_FLAG;  
22     { If set TRUE, two or more tasks require the same  
23       resource. Resource arbitration is done to resolve all  
24       conflicts. }
```

Table 5 -- Multitasking (Build Schedule)

```

1  PROCEDURE BUILD_MULTITASK_SCHEDULE ()
2      { This routine is called a number of times with different
3      seeding to build a statistical sampling of a number of
4      schedules. The calling routine picks the most optimal schedule
5      to run. }
6  BEGIN
7      { Initialize timer and pick a process for first move. For
8      iterative tasks, processes will be started in various orders to
9      seed task builder and establish different scheduling. At each
10     timer tick all processes are examined to check whether it is
11     time to move to next position. If TRUE the task will be
12     entered into the task array at the scheduled time. If more
13     than one process needs movement at the same timer tick, time
14     arbitration ensues. If two or more processes need the same
15     resource, resource arbitration is undergone. This process
16     continues until all tasks in all processes are complete. }
17
18     TIMER = 0;
19     START_FIRST_PROCESS;
20     WHILE NOT ALL_PROCESSES_STARTED DO BEGIN
21         INCREMENT_TIMER_BY 1;
22         IF ANY_TASK_NEEDS_MOVEMENT THEN
23             SET_TASK_MOVE_FLAG
24         ELSE
25             START_NEXT_PROCESS;
26
27         IF MOVE_FLAG > 1 THEN TIME_ARBITRATOR {for multiple moves }
28
29         IF TASK_MOVE THEN ADD_TASK_TO_TASK_ARRAY [TASK_COUNTER]
30     END;
31
32     WHILE NOT ALL_PROCESSES_COMPLETED DO BEGIN
33         INCREMENT_TIMER_BY 1;
34         IF ANY_PROCESS_NEEDS_MOVEMENT THEN SET_TASK_MOVE_FLAG;
35
36         IF MOVE_FLAG > 1 THEN TIME_ARBITRATOR {for multiple moves }
37         IF TASK_MOVE THEN ADD_TASK_ARRAY {TASK} {for resource use }
38     END;
39 END;

```

Table 6 -- Multitasking (Time Arbitrate)

```

PROCEDURE TIME_ARBITRATE ()
{ If two or more processes must be moved simultaneously, the
times are arbitrated, first by examining fuzzy time range and
adjusting those process tasks with fuzzy time. If the
colliding processes are critically timed the processes' prior
tasks are rearranged to circumvent the collision. This
procedure is called in REARRANGE_ARRAY (). }

INTEGER      FUZZY_TIME_COMP the comparison of fuzzy times, maximum value }
BYTE  CRITICAL_FLAG          = 0; { initialize critical flag }
BYTE  CRITICAL_FLAG_ARRAY [5] = { 0, 0, 0, 0, 0 };

BEGIN
  FOR I = 1 TO MAX_PROCESSES
    IF (PROCESS [I].MOVE_FLAG_SET AND FUZZY_TIME [I] <
FUZZY_TIME_COMP) THEN BEGIN
      TASK_MOVE = I; { finds shortest fuzzy time }
      FUZZY_TIME_COMP = FUZZY_TIME [I];
      IF (FUZZY_TIME = 0) THEN BEGIN
        SET CRITICAL_FLAG;
        SET CRITICAL_ARRAY [TASK];
        END;
      END;
      { If two or more processes need to move immediately a
rearrangement of earlier interleaved tasks occurs to
settle conflicts at this point if a fuzzy time range
settle the conflict the process with the shortest fuzzy
time value is set to move. }

      IF CRITICAL_FLAG > 1 THEN REARRANGE_ARRAY ();
      ELSE
        ADD TASK_ARRAY [TASK_MOVE];
    END;
  END;

```

Table 7 -- Multitasking (Resource Arbitrate)

```
1  PROCEDURE RESOURCE_ARBITRATE ()
2      { If two or more processes need the same resource (physical
3        location), fuzzy times for the processes in question are
4        examined to evaluate whether the time slack can settle the
5        conflict. If not, the processes prior tasks are rearranged to
6        circumvent the collision. }
7
8      BYTE CRITICAL_FLAG = 0; { initialize critical flag }
9      BYTE CRITICAL_FLAG_ARRAY [5] = { 0, 0, 0, 0, 0 };
10
11     BEGIN
12     { Compare process task fuzzy time with other process actual
13       task time. }
14
15         COMPARE CRITICAL_PROCESS_1_FUZZY_TIME WITH
16         CRITICAL_PROCESS_2_TASK_TIME;
17         IF >TASK_MOVE = PROCESS_2;
18         ELSE
19         COMPARE CRITICAL_PROCESS_2_FUZZY_TIME WITH
20         CRITICAL_PROCESS_1_TASK_TIME;
21         IF >TASK_MOVE = PROCESS_1;
22         IF TASK_MOVE TRUE
23             ADD TASK_ARRAY [TASK_MOVE];
24         ELSE BEGIN
25             SET CRITICAL_FLAG;
26             SET CRITICAL_FLAG_ARRAY [TASK];
27             REARRANGE_TASK_ARRAY ();
28         END;
29     END;
```

Table 8 -- Multitasking (Rearrange Tasks)

```

PROCEDURE REARRANGE_TASK_ARRAY ()

{ To prevent conflicts which cannot be arbitrated with fuzzy
timing the processes in conflict are examined at their previous
step(s) and timing adjusted in that task to remedy the conflict
at the current task. After time adjustment of the critical
process the task array is reset to the newly adjusted position
and returns to the multitask builder and reworks the rest of
the tasks in all processes. }

BEGIN

{ Find the last time the critical process was moved. }
REPEAT
    POSITION = POSITION - 1;
UNTIL TASK_ARRAY [POSITION] = CRITICAL_FLAG_ARRAY [TASK];

{ Adjust timer. }
INCREMENT TASK [TASK_ARRAY [POSITION].MIN_TIME] BY X;

{ Reset position and time. }
SET POSITION TO CURRENT TASK_ARRAY VALUE;
SET TIMER TO CURRENT TASK_ARRAY VALUE;

RETURN TO MULTITASK_BUILDER;

END;

```

It would be clear to one of ordinary skill in the art, after perusal of the specification, drawings and claims herein, that there is a multitude of interleave paths that can be taken to achieve multitasking of a plurality of processes. Each path will in all probability have a different time to complete all of the steps of all of the processes. In view of this it will be appreciated that for optimum efficiency it is necessary to select the optimum path which will take the minimum time to complete. As a practical matter an iterative process can be used in which the interleave path is computed several times. Each time the interleave variables are iterated they are ordered and computed differently so that different results are obtained for each

1 iteration. The number of iterations necessary to arrive at an
2 optimized path can be computed statistically by taking the number
3 of steps in each task and the number of tasks to be performed.
4 Since run time of the paths calculated from the numerous
5 iterations follow a normal distribution curve, the minimum number
6 of iterations necessary to achieve a path that will be among the
7 faster run times can be calculated.

8
9 One technique for computing an optimal interleave path
10 may compute a set of interleave paths by iterating a selected
11 number of times in response to the number of steps in each task
12 and the number of tasks to be performed. The number of
13 iterations may alternatively be selected to be a fixed number,
14 such as 20 iterations, that may be altered in response to a
15 command from an operator.

16
17 In a preferred embodiment, multiple tasks may be run
18 with disjoint workstations, since it is possible that a reagent,
19 or other chemoactive or bioactive compound or mixture, at a
20 workstation will be contaminated by the sample tissue on the
21 slide. However, where it is believed that contamination would be
22 minimal, or at least that effects of such contamination would be
23 minimal, it would alternatively be preferable to share resources
24 such as standard buffers, washes, and pads. In this alternative
25 embodiment, a source for a standard buffer or wash would be made
26 available by means of an automatic replenisher having a
27 combination of a reservoir and valve, disposed to maintain a
28

1 constant level of liquid available for dipping a slide, similar
2 to a bird feeder.

3
4 In an alternative embodiment, it may be preferable to
5 design protocols for multiple simultaneous tasks to use a maximum
6 set of common reagents or workstations. It would be preferable
7 to design such protocols in two parts, part 1 and part 2,
8 separated by a selected time, so that a set of resources used in
9 part 1 of the protocol are not used in part 2 of the protocol.
10 With this design, a resource arbitration technique may more
11 easily distinguish when it is possible to start a second
12 instantiation of the same protocol.

13 14 APPENDIX

15
16 A preferred set of protocols are shown in an appendix
17 to this specification, hereby incorporated by reference as if
18 fully set forth herein. These protocols are Copyright 1994
19 Biotek Solutions, Inc., and their inclusion in this patent
20 application is not a waiver of copyright or any of the rights
21 afforded by copyright.

22
23 Each protocol is intended for operation on the TechMate
24 (TM) robotic controller (available from Biotek Solutions, Inc. of
25 Santa Barbara, California), and includes the following sections:

- 26
27 o a protocol program name, a brief title, and an expanded
28 title;

- 1 o a summary of the running time;
- 2
- 3 o a description of the principles of operation for the
- 4 protocol;
- 5
- 6 o a description of the nature of the specimen(s) the
- 7 protocol is intended to operate upon;
- 8
- 9 o a description of the nature of the preparation for the
- 10 specimen(s) the protocol is intended to operate upon;
- 11
- 12 o a description of the nature of the preparation for
- 13 chemical reagents the protocol is intended to operate
- 14 with;
- 15
- 16 o a description of the procedure used in operation of the
- 17 protocol;
- 18
- 19 o a description of the expected results from operation of
- 20 the protocol;
- 21
- 22 o a description of references for further information
- 23 about the principles of operation for the protocol;
- 24
- 25 o an ordered listing of program steps; and
- 26
- 27 o a map template for operation of the protocol.
- 28

1 For each protocol, the ordered listing of program steps
2 comprises five columns:

- 3
- 4 o a sequence number, indicating a step number for the
- 5 indicated program step;
- 6
- 7 o a protocol operation name, indicating a protocol
- 8 operation to be performed at the indicated step number;
- 9
- 10 o a minimum time duration, indicating a minimum duration
- 11 the indicated protocol operation may be performed, in
- 12 hours, minutes, and seconds;
- 13
- 14 o a maximum time duration, indicating a maximum duration
- 15 the indicated protocol operation may be performed, in
- 16 hours, minutes, and seconds; and
- 17
- 18 o an indicator of whether the step is actually performed,
- 19 where "Y" = yes and "N" = no; or an oven temperature
- 20 may be designated.
- 21

22 The protocol operation may comprise one of the
23 following:

24		
25	100%	100% ethanol
26	50% EtOH	50% ethanol
27	5N HCL	5 normal hydrochloric acid
28	AALC	absolute alcohol

1	AB1	primary antibody -- AB1A and AB1B also
2		indicate a primary antibody
3	AB2	secondary antibody
4	ABC	avidin biotin conjugate
5	AP	alkaline phosphatase (enzyme detection)
6	BLECH	bleach
7	BLOK	blocking antibody, i.e., a bioactive agent
8		that blocks secondary antibodies that are
9		already present in the robotic system
10	BUFxxx	a phosphate buffer, as noted herein
11	CHROM GEN	a chromagen
12	DAB	diamino benzidine
13	ENZ	an enzyme, e.g., to help open up antigenic
14		sites
15	EOSIN	eosin
16	FK	a fluorescent chromagen
17	H2O	water
18	HEMA	hematoxylin
19	HI WASH	a high stringency (high ionic concentration)
20		wash, typically used for DNA probes
21	HOME	a "home" location for starting and/or
22		stopping an assay protocol
23	HP	HP block, e.g., to block enzymes that are
24		endogenous to the robotic system
25	HYPO	sodium thiosulfate, a reducing agent used to
26		remove some mercury-based fixatives
27	IO	iodine
28	IP	an immunoserum, e.g., for enzyme detection

1 LO WASH a low stringency (low ionic concentration)
2 wash, typically used for DNA probes
3 ME BL methylene blue stain
4 PADxxx a blotter, preferably 1/2 inch thick
5 PARK a location to wait until a next step
6 PROBE a DNA probe
7 SCHIF Schiff reagent for a Schiff reaction
8 STN a stain
9 XY xylene

10

11 Those skilled in the art will recognize, after perusal
12 of this application, that other and further protocol operations,
13 reagents, chemoactive or bioactive compounds, buffers, or other
14 substances would be workable with the devices and substances
15 disclosed herein, and are within the scope and spirit of the
16 invention.

17

18 Alternative Embodiments

19

20 While preferred embodiments are disclosed herein, many
21 variations are possible which remain within the concept, scope,
22 and spirit of the invention, and these variations would become
23 clear to those skilled in the art after perusal of this
24 application.

25

26 For example, it would become clear to those skilled in
27 the art that the devices and techniques described herein would be
28 applicable to other processes, subject to standardization and

1 robotic operation, and that such application would be within the
2 concept, scope, and spirit of the invention. Such processes
3 could include those related to developing film and those related
4 to manufacture or testing of electronic circuits, printed circuit
5 boards, or semiconductor wafers.

6
7 For a second example, it would become clear to those
8 skilled in the art that the devices and techniques described
9 herein for use with liquid would generally be applicable to
10 processes using other flowable substances, including colloids,
11 gels, or powders, and that such application would be within the
12 concept, scope, and spirit of the invention.

CLAIMS

We claim:

1. A method for performing a plurality of independent analysis procedures simultaneously, each said procedure having a sample and at least one process step for operating on that sample, said method comprising

selecting, at a plurality of times, a sample to be moved;

directing a robotic arm to move said sample to be moved by interleaving the process steps of said plurality of independent analysis procedures;

monitoring progress information for said procedures;

and

altering a sequence of said process steps in response to said progress information and in response to information from an operator;

wherein said step of altering comprises the steps of (1) generating a possible new sequence of process steps from a time said altering occurs onward; (2) examining said possible new sequence for possible conflicts; and (3) altering said possible new sequence in response to said timing information and said possible conflicts;

wherein at least one of said process steps comprises a bioassay workstation; a biomedical workstation; a chemical process workstation; a heat process workstation; an irradiation process workstation; a centrifuge, a diffusion device, a

1 distillation device, a separation device; a DNA crosslinking
2 device; an electroporator; a laser device, an optical device; a
3 microwave device, a radioactive sample, a radiation source; an
4 incubation oven, a heating unit; a refrigeration element, a
5 cooling unit; or a workstation in which a process is to be
6 performed comprising at least one of the following substances: an
7 alcohol, an antibody, an antibody carrier, an antibody probe,
8 benzene, cellulose nitrate, chloroform, a chromophore, a colored
9 staining solution, a colorimetric substrate, a counterstain, a
10 dehydrating fluid, a DNA probe, an enzyme labeled detection
11 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
12 fixative for electron microscopy, a fixative for optical
13 microscopy, a fluorescent chromagen, formaldehyde, formalin,
14 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
15 chloride, methacrylate, an organic reagent, osmium tetroxide, a
16 paraffin type wax, picric acid, a plastic substance, a substance
17 on which a selected enzyme is known to have a specified effect, a
18 synthetic dye, toluene, a washing buffer, water, a water soluble
19 dye, a wax, or a test suited to identify a specific chemical
20 substance or enzyme within the tissue sample.

21

22 2. A method for performing a plurality of independent
23 analysis procedures simultaneously, each said procedure having a
24 sample and at least one process step for operating on that
25 sample, said method comprising

26 selecting, at a plurality of times, a sample to be
27 moved;

28

1 directing a robotic arm to move said sample to be moved
2 by interleaving the process steps of said plurality of
3 independent analysis procedures;

4 monitoring progress information for said procedures;
5 and

6 altering a sequence of said process steps in response
7 to said progress information and in response to information from
8 an operator;

9 wherein said step of altering comprises the steps of
10 (1) generating a possible new sequence of process steps from a
11 time said altering occurs onward; (2) examining said possible new
12 sequence for timing conflicts occurring before a known time
13 value, (3) advancing said known time value from the time said
14 altering occurs to an end of said possible new sequence, (4)
15 selecting an exact time to start said first process step when a
16 first process step is found to have a timing conflict with a
17 second process step and said first process step has a range of
18 times at which it may be started, (5) backtracking said known
19 time value and altering said possible new sequence starting from
20 said backtracked known time value to avoid said timing conflict,
21 when a first process step is found to have a timing conflict with
22 a second process step and said first and second process steps
23 have exact times at which they may be started, and (6) signalling
24 an error when said known time value is backtracked beyond the
25 time said altering occurs;

26 wherein at least one of said process steps comprises a
27 bioassay workstation; a biomedical workstation; a chemical
28 process workstation; a heat process workstation; an irradiation

1 process workstation; a centrifuge, a diffusion device, a
2 distillation device, a separation device; a DNA crosslinking
3 device; an electroporator; a laser device, an optical device; a
4 microwave device, a radioactive sample, a radiation source; an
5 incubation oven, a heating unit; a refrigeration element, a
6 cooling unit; or a workstation in which a process is to be
7 performed comprising at least one of the following substances: an
8 alcohol, an antibody, an antibody carrier, an antibody probe,
9 benzene, cellulose nitrate, chloroform, a chromophore, a colored
10 staining solution, a colorimetric substrate, a counterstain, a
11 dehydrating fluid, a DNA probe, an enzyme labeled detection
12 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
13 fixative for electron microscopy, a fixative for optical
14 microscopy, a fluorescent chromagen, formaldehyde, formalin,
15 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
16 chloride, methacrylate, an organic reagent, osmium tetroxide, a
17 paraffin type wax, picric acid, a plastic substance, a substance
18 on which a selected enzyme is known to have a specified effect, a
19 synthetic dye, toluene, a washing buffer, water, a water soluble
20 dye, a wax, or a test suited to identify a specific chemical
21 substance or enzyme within the tissue sample.

22

23 3. A method for performing a plurality of independent
24 analysis procedures simultaneously, each said procedure having a
25 sample and at least one process step for operating on that
26 sample, said method comprising the steps of

27 selecting, at a plurality of times, a sample to be
28 moved, said step of selecting comprising the steps of (1)

1 generating a plurality of possible sequences of process steps,
2 less than all possible sequences, (2) determining statistical
3 information about a time distribution of said plurality, (3)
4 selecting a preferred one of said plurality with a desired total
5 expected time, so as to substantially minimize a total time
6 required to complete said procedures, and (4) selecting said
7 sample to be moved in accordance with said preferred one of said
8 plurality of possible sequences;

9 directing a robotic arm to move said sample to be moved
10 by interleaving the process steps of said plurality of
11 independent analysis procedures;

12 wherein at least one of said process steps comprises a
13 bioassay workstation; a biomedical workstation; a chemical
14 process workstation; a heat process workstation; an irradiation
15 process workstation; a centrifuge; a diffusion device, a
16 distillation device, a separation device; a DNA crosslinking
17 device; an electroporator; a laser device, an optical device; a
18 microwave device, a radioactive sample, a radiation source; an
19 incubation oven, a heating unit; a refrigeration element, a
20 cooling unit; or a workstation in which a process is to be
21 performed comprising at least one of the following substances: an
22 alcohol, an antibody, an antibody carrier, an antibody probe,
23 benzene, cellulose nitrate, chloroform, a chromophore, a colored
24 staining solution, a colorimetric substrate, a counterstain, a
25 dehydrating fluid, a DNA probe, an enzyme labeled detection
26 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
27 fixative for electron microscopy, a fixative for optical
28 microscopy, a fluorescent chromagen, formaldehyde, formalin,

1 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
2 chloride, methacrylate, an organic reagent, osmium tetroxide, a
3 paraffin type wax, picric acid, a plastic substance, a substance
4 on which a selected enzyme is known to have a specified effect, a
5 synthetic dye, toluene, a washing buffer, water, a water soluble
6 dye, a wax, or a test suited to identify a specific chemical
7 substance or enzyme within the tissue sample.

8
9 4. A method of operating a processor having a display
10 screen for specifying a test procedure in a system for performing
11 a plurality of simultaneous test procedures, said method
12 comprising the steps of

13 displaying a plurality of templates on said screen for
14 viewing by an operator;

15 receiving a first signal from said operator indicative
16 of a first location on said screen;

17 identifying said location with a first one of said
18 templates;

19 receiving a second signal from said operator indicative
20 of a second location on said screen;

21 displaying said first one of said templates at said
22 second location;

23 identifying a process step with said template and said
24 second location;

25 identifying a location and order for said process step
26 to be performed in response to said second location; and

27 repeatedly performing said steps until an ordered
28 sequence of said process steps has been determined.

1 5. A method as in claim 4, comprising the step of
2 receiving a third signal from said operator indicative of
3 information about said process step.
4

5 6. A method of operating a processor having a display
6 screen for specifying a test procedure in a system for performing
7 a plurality of test procedures, said method comprising the steps
8 of

9 selecting a first location on said screen within a
10 template displayed on a screen;

11 moving a copy of said template to a second location on
12 said screen;

13 identifying a process step with said template and said
14 second location;

15 identifying a location and order for said process step
16 to be performed in response to said second location; and

17 repeatedly performing said steps until an ordered
18 sequence of said process steps has been determined.
19

20 7. A method of operating a system for performing a
21 plurality of independent analysis procedures simultaneously, each
22 said procedure having a sample and at least one process step for
23 operating on that sample, said method comprising

24 coupling a plurality of tiles to a substrate, each at a
25 selected location on said substrate;

26 coupling a plurality of sealed reagent trays, each
27 having a substantially uniform shape and size selected from a
28 predetermined set of shapes and sizes, each having been prefilled

1 with an amount of a substance, said amount and said substance
2 selected from a predetermined set of amounts and substances, to
3 said plurality of tiles;

4 exposing said substance in said sealed reagent trays
5 while said sealed reagent trays are coupled to said plurality of
6 tiles;

7 selecting a plurality of analysis programs from a set
8 of predetermined analysis programs stored in a computer memory;
9 and

10 initiating an interleaving program stored in a computer
11 memory that performs said plurality of analysis programs
12 simultaneously by directing a robotic device to move said samples
13 among said plurality of reagent trays, interleaving a plurality
14 of steps of said analysis programs.

15

16 8. A method for performing a plurality of independent
17 analysis procedures simultaneously, each said procedure having a
18 sample and at least one process step for operating on that
19 sample, said method comprising

20 disposing said sample in a slide holder, said slide
21 holder comprising a set of slides disposed in an array;

22 disposing said slide holder in an incubation chamber
23 having a plurality of heat exchanger elements disposed in an
24 array matched to said slides;

25 applying a selected amount of a hydration fluid to said
26 sample; and

27

28

1 applying a regulated amount of energy to said heat
2 exchanger elements to achieve a selected temperature at said
3 sample.

4
5 9. A method as in claim 8, comprising adjusting a set
6 of ventilation openings coupled to said incubation chamber.

7
8 10. A method as in claim 8, comprising cooling said
9 incubation chamber while said slides are disposed therein.

10
11 11. A method as in claim 10, wherein said step of
12 cooling comprises operating a fan using a temperature regulator.

13
14 12. A method as in claim 8, comprising disposing a
15 structural member near said slides to direct condensation away
16 from said slides.

17
18 13. A method as in claim 8, wherein said step of
19 applying a regulated amount of energy comprises cooling said
20 incubation chamber.

21
22 14. A method as in claim 8, wherein said step of
23 applying a selected amount of a hydration fluid comprises
24 maintaining a level of hydration fluid in a fluid well coupled to
25 said incubation chamber at a selected level.

26
27 15. A method as in claim 8, wherein said step of
28 applying a selected amount of a hydration fluid comprises

1 applying a hydration fluid having about .1% to about 3% of a
2 surfactant.

3

4 16. A method as in claim 8, wherein said step of
5 applying a selected amount of a hydration fluid comprises
6 applying a hydration fluid having less than about 3% of a
7 surfactant.

8

9 17. A system for performing a plurality of independent
10 analysis procedures simultaneously, each said procedure having a
11 sample and at least one process step for operating on that
12 sample, said system comprising

13 a robotic arm for moving the samples among a plurality
14 of processing stations;

15 a processor for selecting, at a plurality of times, a
16 sample to be moved, and for directing said robotic arm to move
17 said sample to be moved; said processor having means for
18 directing said robotic arm to interleave the process steps of
19 said plurality of independent analysis procedures;

20 means for monitoring progress information for said
21 procedures; and

22 means for altering a sequence of said process steps in
23 response to said progress information and in response to
24 information from an operator;

25 wherein said means for altering comprises (1) means for
26 generating a possible new sequence of process steps from a time
27 said altering occurs onward; (2) means for examining said
28 possible new sequence for possible conflicts; and (3) means for

1 altering said possible new sequence in response to said timing
2 information and said possible conflicts;
3 wherein at least one of said process steps comprises a
4 bioassay workstation; a biomedical workstation; a chemical
5 process workstation; a heat process workstation; an irradiation
6 process workstation; a centrifuge, a diffusion device, a
7 distillation device, a separation device; a DNA crosslinking
8 device; an electroporator; a laser device, an optical device; a
9 microwave device, a radioactive sample, a radiation source; an
10 incubation oven, a heating unit; a refrigeration element, a
11 cooling unit; or a workstation in which a process is to be
12 performed comprising at least one of the following substances: an
13 alcohol, an antibody, an antibody carrier, an antibody probe,
14 benzene, cellulose nitrate, chloroform, a chromophore, a colored
15 staining solution, a colormetric substrate, a counterstain, a
16 dehydrating fluid, a DNA probe, an enzyme labeled detection
17 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
18 fixative for electron microscopy, a fixative for optical
19 microscopy, a fluorescent chromagen, formaldehyde, formalin,
20 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
21 chloride, methacrylate, an organic reagent, osmium tetroxide, a
22 paraffin type wax, picric acid, a plastic substance, a substance
23 on which a selected enzyme is known to have a specified effect, a
24 synthetic dye, toluene, a washing buffer, water, a water soluble
25 dye, a wax, or a test suited to identify a specific chemical
26 substance or enzyme within the tissue sample.

1 18. A system for performing a plurality of independent
2 analysis procedures simultaneously, each said procedure having a
3 sample and at least one process step for operating on that
4 sample, said system comprising

5 a robotic arm for moving the samples among a plurality
6 of processing stations;

7 a processor for selecting, at a plurality of times, a
8 sample to be moved, and for directing said robotic arm to move
9 said sample to be moved; said processor having means for
10 directing said robotic arm to interleave the process steps of
11 said plurality of independent analysis procedures;

12 means for monitoring progress information for said
13 procedures; and

14 means for altering a sequence of said process steps in
15 response to said progress information and in response to
16 information from an operator;

17 wherein said means for altering comprises (1) means for
18 generating a possible new sequence of process steps from a time
19 said altering occurs onward; (2) means for examining said
20 possible new sequence for timing conflicts occurring before a
21 known time value, (3) means for advancing said known time value
22 from the time said altering occurs to an end of said possible new
23 sequence, (4) means, when a first process step is found to have a
24 timing conflict with a second process step and said first process
25 step has a range of times at which it may be started, for
26 selecting an exact time to start said first process step, (5)
27 means, when a first process step is found to have a timing
28 conflict with a second process step and said first and second

1 process steps have exact times at which they may be started, for
2 backtracking said known time value and altering said possible new
3 sequence starting from said backtracked known time value to avoid
4 said timing conflict, and (6) means for signalling an error when
5 said known time value is backtracked beyond the time said
6 altering occurs;

7 wherein at least one of said process steps comprises a
8 bioassay workstation; a biomedical workstation; a chemical
9 process workstation; a heat process workstation; an irradiation
10 process workstation; a centrifuge, a diffusion device, a
11 distillation device, a separation device; a DNA crosslinking
12 device; an electroporator; a laser device, an optical device; a
13 microwave device, a radioactive sample, a radiation source; an
14 incubation oven, a heating unit; a refrigeration element, a
15 cooling unit; or a workstation in which a process is to be
16 performed comprising at least one of the following substances: an
17 alcohol, an antibody, an antibody carrier, an antibody probe,
18 benzene, cellulose nitrate, chloroform, a chromophore, a colored
19 staining solution, a colormetric substrate, a counterstain, a
20 dehydrating fluid, a DNA probe, an enzyme labeled detection
21 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
22 fixative for electron microscopy, a fixative for optical
23 microscopy, a fluorescent chromagen, formaldehyde, formalin,
24 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
25 chloride, methacrylate, an organic reagent, osmium tetroxide, a
26 paraffin type wax, picric acid, a plastic substance, a substance
27 on which a selected enzyme is known to have a specified effect, a
28 synthetic dye, toluene, a washing buffer, water, a water soluble

1 dye, a wax, or a test suited to identify a specific chemical
2 substance or enzyme within the tissue sample.

3
4 19. A system for performing a plurality of independent
5 analysis procedures simultaneously, each said procedure having a
6 sample and at least one process step for operating on that
7 sample, said system comprising

8 a robotic arm for moving the samples among a plurality
9 of processing stations; and

10 a processor for selecting, at a plurality of times, a
11 sample to be moved, and for directing said robotic arm to move
12 said sample to be moved; said processor having means for
13 directing said robotic arm to interleave the process steps of
14 said plurality of independent analysis procedures;

15 wherein said processor comprises

16 a display screen showing a set of predetermined symbols
17 representing process steps;

18 means for drawing one of said symbols on said display
19 screen in response to information from an operator;

20 means for associating a process step with a location
21 where said process step is to be performed; and

22 means for associating a processing station with said
23 one symbol;

24 wherein at least one of said process steps comprises a
25 bioassay workstation; a biomedical workstation; a chemical
26 process workstation; a heat process workstation; an irradiation
27 process workstation; a centrifuge, a diffusion device, a
28 distillation device, a separation device; a DNA crosslinking

1 device; an electroporator; a laser device, an optical device; a
2 microwave device, a radioactive sample, a radiation source; an
3 incubation oven, a heating unit; a refrigeration element, a
4 cooling unit; or a workstation in which a process is to be
5 performed comprising at least one of the following substances: an
6 alcohol, an antibody, an antibody carrier, an antibody probe,
7 benzene, cellulose nitrate, chloroform, a chromophore, a colored
8 staining solution, a colormetric substrate, a counterstain, a
9 dehydrating fluid, a DNA probe, an enzyme labeled detection
10 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
11 fixative for electron microscopy, a fixative for optical
12 microscopy, a fluorescent chromagen, formaldehyde, formalin,
13 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
14 chloride, methacrylate, an organic reagent, osmium tetroxide, a
15 paraffin type wax, picric acid, a plastic substance, a substance
16 on which a selected enzyme is known to have a specified effect, a
17 synthetic dye, toluene, a washing buffer, water, a water soluble
18 dye, a wax, or a test suited to identify a specific chemical
19 substance or enzyme within the tissue sample.

20
21 20. A system for performing a plurality of independent
22 analysis procedures simultaneously, each said procedure having a
23 sample and at least one process step for operating on that
24 sample, said system comprising

25 a robotic arm for moving the samples among a plurality
26 of processing stations; and

27 a processor for selecting, at a plurality of times, a
28 sample to be moved, and for directing said robotic arm to move

1 said sample to be moved; said processor having means for
2 directing said robotic arm to interleave the process steps of
3 said plurality of independent analysis procedures;
4 wherein said processor comprises
5 a memory for storing timing information for each said
6 process step, said timing information comprising a predetermined
7 range of durations during which said process step may be in a
8 predetermined state; and
9 means for determining an exact time to start each said
10 process step in a first said procedure in response to timing
11 information comprising for at least one step in a second said
12 procedure;
13 wherein at least one of said process steps comprises a
14 bioassay workstation; a biomedical workstation; a chemical
15 process workstation; a heat process workstation; an irradiation
16 process workstation; a centrifuge, a diffusion device, a
17 distillation device, a separation device; a DNA crosslinking
18 device; an electroporator; a laser device, an optical device; a
19 microwave device, a radioactive sample, a radiation source; an
20 incubation oven, a heating unit; a refrigeration element, a
21 cooling unit; or a workstation in which a process is to be
22 performed comprising at least one of the following substances: an
23 alcohol, an antibody, an antibody carrier, an antibody probe,
24 benzene, cellulose nitrate, chloroform, a chromophore, a colored
25 staining solution, a colormetric substrate, a counterstain, a
26 dehydrating fluid, a DNA probe, an enzyme labeled detection
27 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
28 fixative for electron microscopy, a fixative for optical

1 device; an electroporator; a laser device, an optical device; a
2 microwave device, a radioactive sample, a radiation source; an
3 incubation oven, a heating unit; a refrigeration element, a
4 cooling unit; or a workstation in which a process is to be
5 performed comprising at least one of the following substances: an
6 alcohol, an antibody, an antibody carrier, an antibody probe,
7 benzene, cellulose nitrate, chloroform, a chromophore, a colored
8 staining solution, a colormetric substrate, a counterstain, a
9 dehydrating fluid, a DNA probe, an enzyme labeled detection
10 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
11 fixative for electron microscopy, a fixative for optical
12 microscopy, a fluorescent chromagen, formaldehyde, formalin,
13 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
14 chloride, methacrylate, an organic reagent, osmium tetroxide, a
15 paraffin type wax, picric acid, a plastic substance, a substance
16 on which a selected enzyme is known to have a specified effect, a
17 synthetic dye, toluene, a washing buffer, water, a water soluble
18 dye, a wax, or a test suited to identify a specific chemical
19 substance or enzyme within the tissue sample.

20
21 20. A system for performing a plurality of independent
22 analysis procedures simultaneously, each said procedure having a
23 sample and at least one process step for operating on that
24 sample, said system comprising

25 a robotic arm for moving the samples among a plurality
26 of processing stations; and

27 a processor for selecting, at a plurality of times, a
28 sample to be moved, and for directing said robotic arm to move

1 said sample to be moved; said processor having means for
2 directing said robotic arm to interleave the process steps of
3 said plurality of independent analysis procedures;
4 wherein said processor comprises
5 a memory for storing timing information for each said
6 process step, said timing information comprising a predetermined
7 range of durations during which said process step may be in a
8 predetermined state; and
9 means for determining an exact time to start each said
10 process step in a first said procedure in response to timing
11 information comprising for at least one step in a second said
12 procedure;
13 wherein at least one of said process steps comprises a
14 bioassay workstation; a biomedical workstation; a chemical
15 process workstation; a heat process workstation; an irradiation
16 process workstation; a centrifuge, a diffusion device, a
17 distillation device, a separation device; a DNA crosslinking
18 device; an electroporator; a laser device, an optical device; a
19 microwave device, a radioactive sample, a radiation source; an
20 incubation oven, a heating unit; a refrigeration element, a
21 cooling unit; or a workstation in which a process is to be
22 performed comprising at least one of the following substances: an
23 alcohol, an antibody, an antibody carrier, an antibody probe,
24 benzene, cellulose nitrate, chloroform, a chromophore, a colored
25 staining solution, a colormetric substrate, a counterstain, a
26 dehydrating fluid, a DNA probe, an enzyme labeled detection
27 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
28 fixative for electron microscopy, a fixative for optical

1 microscopy, a fluorescent chromagen, formaldehyde, formalin,
2 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
3 chloride, methacrylate, an organic reagent, osmium tetroxide, a
4 paraffin type wax, picric acid, a plastic substance, a substance
5 on which a selected enzyme is known to have a specified effect, a
6 synthetic dye, toluene, a washing buffer, water, a water soluble
7 dye, a wax, or a test suited to identify a specific chemical
8 substance or enzyme within the tissue sample.

9
10 21. A system for performing a plurality of independent
11 analysis procedures simultaneously, each said procedure having a
12 sample and at least one process step for operating on that
13 sample, said system comprising

14 a robotic arm for moving the samples among a plurality
15 of processing stations; and

16 a processor for selecting, at a plurality of times, a
17 sample to be moved, and for directing said robotic arm to move
18 said sample to be moved; said processor having means for
19 directing said robotic arm to interleave the process steps of
20 said plurality of independent analysis procedures;

21 wherein said processor comprises

22 means for generating a plurality of possible sequences
23 of process steps, less than all possible sequences;

24 means for determining statistical information about a
25 time distribution of said plurality; and

26 means for selecting one of said plurality with a
27 desired total expected time, so as to substantially minimize a
28 total time required to complete said procedures;

1 wherein at least one of said process steps comprises a
2 bioassay workstation; a biomedical workstation; a chemical
3 process workstation; a heat process workstation; an irradiation
4 process workstation; a centrifuge, a diffusion device, a
5 distillation device, a separation device; a DNA crosslinking
6 device; an electroporator; a laser device, an optical device; a
7 microwave device, a radioactive sample, a radiation source; an
8 incubation oven, a heating unit; a refrigeration element, a
9 cooling unit; or a workstation in which a process is to be
10 performed comprising at least one of the following substances: an
11 alcohol, an antibody, an antibody carrier, an antibody probe,
12 benzene, cellulose nitrate, chloroform, a chromophore, a colored
13 staining solution, a colormetric substrate, a counterstain, a
14 dehydrating fluid, a DNA probe, an enzyme labeled detection
15 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
16 fixative for electron microscopy, a fixative for optical
17 microscopy, a fluorescent chromagen, formaldehyde, formalin,
18 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
19 chloride, methacrylate, an organic reagent, osmium tetroxide, a
20 paraffin type wax, picric acid, a plastic substance, a substance
21 on which a selected enzyme is known to have a specified effect, a
22 synthetic dye, toluene, a washing buffer, water, a water soluble
23 dye, a wax, or a test suited to identify a specific chemical
24 substance or enzyme within the tissue sample.

25
26 22. A system for performing a plurality of independent
27 analysis procedures simultaneously, each said procedure having a
28

1 sample and at least one process step for operating on that
2 sample, said system comprising
3 a robotic arm for moving the samples among a plurality
4 of processing stations; and
5 a processor for selecting, at a plurality of times, a
6 sample to be moved, and for directing said robotic arm to move
7 said sample to be moved; said processor having means for
8 directing said robotic arm to interleave the process steps of
9 said plurality of independent analysis procedures;
10 wherein said processor comprises
11 means for monitoring dynamic progress information for
12 said procedures; and
13 means for altering a sequence of said process steps in
14 response to said progress information and in response to
15 information from an operator;
16 wherein at least one of said process steps comprises a
17 bioassay workstation; a biomedical workstation; a chemical
18 process workstation; a heat process workstation; an irradiation
19 process workstation; a centrifuge, a diffusion device, a
20 distillation device, a separation device; a DNA crosslinking
21 device; an electroporator; a laser device, an optical device; a
22 microwave device, a radioactive sample, a radiation source; an
23 incubation oven, a heating unit; a refrigeration element, a
24 cooling unit; or a workstation in which a process is to be
25 performed comprising at least one of the following substances: an
26 alcohol, an antibody, an antibody carrier, an antibody probe,
27 benzene, cellulose nitrate, chloroform, a chromophore, a colored
28 staining solution, a colormetric substrate, a counterstain, a

1 dehydrating fluid, a DNA probe, an enzyme labeled detection
2 system, eosin, epoxy resin, ester wax, ethanol, a fat solvent, a
3 fixative for electron microscopy, a fixative for optical
4 microscopy, a fluorescent chromagen, formaldehyde, formalin,
5 glutaraldehyde, hematoxylin, a heavy metal salt, mercuric
6 chloride, methacrylate, an organic reagent, osmium tetroxide, a
7 paraffin type wax, picric acid, a plastic substance, a substance
8 on which a selected enzyme is known to have a specified effect, a
9 synthetic dye, toluene, a washing buffer, water, a water soluble
10 dye, a wax, or a test suited to identify a specific chemical
11 substance or enzyme within the tissue sample.
12

13 23. A system for performing a plurality of independent
14 analysis procedures simultaneously, each said procedure having a
15 sample and at least one process step for operating on that
16 sample, said system comprising

17 a robotic device for moving the samples among a
18 plurality of processing stations; and

19 a processor for selecting, at a plurality of times, a
20 sample to be moved, and for directing said robotic arm to move
21 said sample to be moved; said processor having means for
22 directing said robotic arm to interleave the process steps of
23 said plurality of independent analysis procedures in a sequence
24 conforming to a predetermined range of durations for each one of
25 said process steps.
26

27 24. A system as in claim 23, comprising a data
28 structure having a sequence of process steps indexed by a time

1 value and indicating a range of possible durations for each said
2 process step.

3
4 25. A system as in claim 23, comprising
5 a display area for specifying a test procedure;
6 means for selecting a first location on said display
7 area within a template displayed thereon;
8 means for moving a copy of said template to a second
9 location on said display area; and
10 means for identifying a process step and a sequence
11 order for said process step, in response to said template and
12 said second location.

13
14 26. A system as in claim 23, comprising
15 means for monitoring dynamic progress information for
16 said plurality of independent procedures; and
17 means for altering a sequence of said process steps in
18 response to said progress information and in response to
19 information from an operator.

20
21 27. A system as in claim 26, wherein said means for
22 altering comprises
23 means for receiving a command from said operator for
24 changing said sequence of process steps; and
25 means for determining a new sequence of process steps
26 in response to said command and in response to timing information
27 about said process steps.

28

1 28. A system as in claim 23, wherein at least one of
2 said process steps comprises a bioassay workstation; a biomedical
3 workstation; a chemical process workstation; a heat process
4 workstation; an irradiation process workstation; a centrifuge, a
5 diffusion device, a distillation device, a separation device; a
6 DNA crosslinking device; an electroporator; a laser device, an
7 optical device; a microwave device, a radioactive sample, a
8 radiation source; an incubation oven, a heating unit; a
9 refrigeration element, a cooling unit; or a workstation in which
10 a process is to be performed comprising at least one of the
11 following substances: an alcohol, an antibody, an antibody
12 carrier, an antibody probe, benzene, cellulose nitrate,
13 chloroform, a chromophore, a colored staining solution, a
14 colormetric substrate, a counterstain, a dehydrating fluid, a DNA
15 probe, an enzyme labeled detection system, eosin, epoxy resin,
16 ester wax, ethanol, a fat solvent, a fixative for electron
17 microscopy, a fixative for optical microscopy, a fluorescent
18 chromagen, formaldehyde, formalin, glutaraldehyde, hematoxylin, a
19 heavy metal salt, mercuric chloride, methacrylate, an organic
20 reagent, osmium tetroxide, a paraffin type wax, picric acid, a
21 plastic substance, a substance on which a selected enzyme is
22 known to have a specified effect, a synthetic dye, toluene, a
23 washing buffer, water, a water soluble dye, a wax, or a test
24 suited to identify a specific chemical substance or enzyme within
25 the tissue sample.

1 29. A system as in claim 23, wherein said plurality of
2 processing stations are disposed in a set of grid locations, and
3 wherein said robotic device comprises

4 a bench robot with sufficient degrees of freedom that
5 it is able to reach each of said plurality of processing stations
6 with suitable movement;

7 means for coupling to a sample;

8 means for holding a sample while moving; and

9 means for decoupling from a sample.

10
11 30. A system as in claim 23, wherein said processor
12 comprises

13 a memory for storing timing information for each said
14 process step, said timing information comprising a range of
15 durations during which said process step may be in a
16 predetermined state; and

17 means for determining an exact time to start each said
18 process step in a first said procedure in response to timing
19 information for at least one process step in a second said
20 procedure.

21
22 31. A system as in claim 30, wherein said means for
23 determining comprises

24 means for generating a possible sequence of process
25 steps;

26 means for examining said possible sequence for timing
27 conflicts occurring before a known time value;

28

1 means for advancing said known time value from a
2 beginning of said possible sequence to an end of said possible
3 sequence;

4 means, when a first process step is found to have a
5 timing conflict with a second process step and said first process
6 step has a range of times at which it may be started, for
7 selecting an exact time to start said first process step; and

8 means, when a first process step is found to have a
9 timing conflict with a second process step and said first and
10 second process steps have exact times at which they may be
11 started, for backtracking said known time value and altering said
12 possible sequence starting from said backtracked known time value
13 to avoid said timing conflict.

14
15 32. A system as in claim 23, wherein said processor
16 comprises

17 means for generating a plurality of possible sequences
18 of process steps, less than all possible sequences;

19 means for determining statistical information about a
20 time distribution of said plurality of possible sequences; and

21 means for selecting one of said plurality of possible
22 sequences with a desired total expected time, so as to
23 substantially minimize a total time required to complete said
24 procedures.

25
26 33. A system as in claim 23, wherein said robotic
27 device comprises
28

1 a substrate to which are coupled a plurality of tiles,
2 each one of said tiles disposed at a selected location on said
3 substrate;

4 a plurality of reagent trays coupled to said plurality
5 of tiles, each one of said reagent trays having substantially
6 identical shape and size;

7 a robotic arm disposed for reaching substantially all
8 of said tiles and comprising means for coupling to and decoupling
9 from a sample holder, said sample holder having means for holding
10 at least one sample in a selected position, whereby said robotic
11 arm is capable of moving said sample from a first one of said
12 reagent trays to a second one of said reagent trays.

13
14 34. A system as in claim 33, wherein
15 each one of said tiles comprises a plurality of
16 receptacles, each receptacle for receiving one of said plurality
17 of reagent trays.

18
19 35. A system as in claim 33, wherein
20 said first one reagent tray comprises a cover disposed
21 thereon with adhering means having sufficient power to prevent
22 release of said cover during normal handling and shipping, but
23 able to release said cover when said reagent tray is locked into
24 said tile with said reagent tray lock.

25
26 36. A system as in claim 33, wherein
27
28

1 said first one reagent tray comprises a plurality of
2 receptacles, each for an aliquot of a substance for reaction with
3 said sample;

4 a first said receptacle and an second said receptacle
5 define a barrier disposed to prevent said substance from moving
6 from said first said receptacle to said second said receptacle
7 when said reagent tray is disposed in a first position, and
8 disposed to not prevent said substance from moving from said
9 first said receptacle to said second said receptacle when said
10 reagent tray is disposed in a second position.

11
12 37. A system as in claim 33, wherein

13 said first one reagent tray comprises a plurality of
14 receptacles, each for an aliquot of a substance for reaction with
15 said sample;

16 a first said receptacle and an second said receptacle
17 define a barrier disposed to prevent said substance from moving
18 from said first said receptacle to said second said receptacle
19 when said reagent tray is disposed in a first position and said
20 aliquot is less than a selected amount, and disposed to not
21 prevent said substance from moving from said first said
22 receptacle to said second said receptacle when said reagent tray
23 is disposed in said first position and said aliquot is greater
24 than said selected amount.

25
26 38. A system as in claim 37, wherein said selected
27 amount is just large enough to cover said sample mounted on a
28 slide by capillary action.

1 39. A system as in claim 33, wherein
2 said first one reagent tray comprises a plurality of
3 receptacles, each for an aliquot of a substance for reaction with
4 said sample;
5 said sample holder comprises means for holding a
6 plurality of samples; and
7 each said receptacle is disposed to receive exactly one
8 of said plurality of samples coupled to a sample holder when said
9 sample holder is disposed adjacent to said tile.

10

11 40. A system as in claim 33, wherein said first one
12 reagent tray comprises a receptacle for an aliquot of a substance
13 for reaction with said sample, said receptacle having a
14 surface/volume ratio low enough to minimize evaporation of said
15 substance.

16

17 41. A system as in claim 33, wherein said first one
18 reagent tray comprises a receptacle for an aliquot of a substance
19 for reaction with said sample, said aliquot having a volume just
20 large enough to cover said sample mounted on a slide by capillary
21 action.

22

23 42. A system as in claim 33, wherein said first one
24 reagent tray comprises a receptacle for an aliquot of a substance
25 for reaction with said sample, said receptacle having a volume
26 just large enough to receive a slide comprising said sample.

27

28 43. A system as in claim 33, wherein

1 said first one reagent tray comprises a rectilinear
2 external form with a reagent tray lock coupled thereto;

3 said first one reagent tray is disposed for coupling to
4 a first one of said plurality of tiles, said first one tile
5 having a tray receptacle defining a rectilinear region into which
6 said rectilinear external form may just fit;

7 said tray receptacle comprises a lock receptacle for
8 receiving said reagent tray lock, said lock receptacle defining a
9 void disposed near said rectilinear region into which said
10 reagent tray lock may just fit; and

11 said reagent tray lock is disposed to just fit into
12 said void when said reagent tray is just fit into said tray
13 receptacle.

14
15 44. A system as in claim 43, wherein

16 said reagent tray lock comprises a spring member
17 coupled to said rectilinear external form, and a lip member
18 protruding from said rectilinear external form; and

19 said lip member is disposed to just fit into said void
20 when said reagent tray is just fit into said tray receptacle, and
21 said lip member is disposed to prevent release of said reagent
22 tray from said tile in response to a vertical force.

23
24 45. A system as in claim 44, wherein

25 said reagent tray comprises a second member protruding
26 from said rectilinear external form;

27 said tray receptacle comprises a second receptacle for
28 receiving said second member, said second receptacle defining a

1 second void disposed near said rectilinear region into which said
2 second member may just fit;

3 said second member is disposed to just fit into said
4 second void when said reagent tray is just fit into said tray
5 receptacle; and

6 said reagent tray lock is disposed to allow release of
7 said reagent tray from said tile in response to horizontal force
8 combined with a vertical force.

9

10 46. A system as in claim 33, wherein

11 said first one reagent tray is coupled to a first one
12 of said plurality of tiles; and

13 said first one reagent tray comprises a lock coupled to
14 said first one tile.

15

16 47. A system as in claim 23, wherein said robotic
17 device comprises

18 a substrate to which are coupled a plurality of
19 workstations, each one of said workstations disposed at a
20 selected location on said substrate and each said workstation
21 having been prefilled with an amount of a substance, said amount
22 and said substance selected from a predetermined set of amounts
23 and substances;

24 a plurality of analysis programs from a set of
25 predetermined analysis programs stored in a computer memory; and

26 an interleaving program stored in a computer memory
27 that performs said plurality of analysis programs simultaneously
28 by directing a robotic device to move said samples among said

1 plurality of reagent trays, interleaving a plurality of steps of
2 said analysis programs.

3
4 48. A system as in claim 23, wherein said robotic
5 device comprises

6 a substrate to which are coupled a plurality of
7 workstations, each one of said workstations disposed at a
8 selected location on said substrate and each said workstation
9 having been prefilled with an amount of a substance, said amount
10 and said substance selected from a predetermined set of amounts
11 and substances;

12 a robotic arm disposed for reaching substantially all
13 of said tiles and comprising means for coupling to and decoupling
14 from a sample holder, said sample holder having means for holding
15 at least one sample in a selected position, whereby said robotic
16 arm is capable of moving said sample from a first one of said
17 workstations to a second one of said workstations.

18
19 49. A system for performing a plurality of independent
20 analysis procedures simultaneously, each said procedure having a
21 sample and at least one process step for operating on that
22 sample, said system comprising

23 means for coupling a plurality of tiles to a substrate,
24 each at a selected location on said substrate;

25 means for coupling a plurality of sealed reagent trays,
26 each having a substantially uniform shape and size selected from
27 a predetermined set of shapes and sizes, each having been
28 prefilled with an amount of a substance, said amount and said

1 substance selected from a predetermined set of amounts and
2 substances, to said plurality of tiles;
3 means for exposing said substance in said sealed
4 reagent trays while said sealed reagent trays are coupled to said
5 plurality of tiles;
6 means for selecting a plurality of analysis programs
7 from a set of predetermined analysis programs stored in a
8 computer memory; and
9 means for initiating an interleaving program stored in
10 a computer memory that performs said plurality of analysis
11 programs simultaneously by directing a robotic device to move
12 said samples among said plurality of reagent trays, interleaving
13 a plurality of steps of said analysis programs.

14
15 50. In a system for performing a plurality of
16 independent analysis procedures simultaneously, each said
17 procedure having a sample and at least one process step for
18 operating on that sample, a combination of a reagent tray and a
19 tile comprising
20 a reagent tray lock having a spring disposed on said
21 reagent tray and a receiving element for said spring disposed on
22 said tile;
23 a cover disposed on said reagent tray with adhering
24 means having sufficient power to prevent release of said cover
25 during normal handling and shipping, but able to release said
26 cover when said reagent tray is locked into said tile with said
27 reagent tray lock.

28

1 51. A combination as in claim 50, wherein
2 said reagent tray comprises a plurality of receptacles,
3 each for an aliquot of a substance for reaction with a sample;
4 a first said receptacle and an second said receptacle
5 define a barrier disposed to prevent said substance from moving
6 from said first said receptacle to said second said receptacle
7 when said reagent tray is disposed in a first position, and
8 disposed to not prevent said substance from moving from said
9 first said receptacle to said second said receptacle when said
10 reagent tray is disposed in a second position.

11
12 52. A combination as in claim 50, wherein
13 said reagent tray comprises a plurality of receptacles,
14 each for an aliquot of a substance for reaction with a sample;
15 a first said receptacle and an second said receptacle
16 define a barrier disposed to prevent said substance from moving
17 from said first said receptacle to said second said receptacle
18 when said reagent tray is disposed in a first position and said
19 aliquot is less than a selected amount, and disposed to not
20 prevent said substance from moving from said first said
21 receptacle to said second said receptacle when said reagent tray
22 is disposed in said first position and said aliquot is greater
23 than said selected amount.

24
25 53. A combination as in claim 52, wherein said
26 selected amount is just large enough to cover said sample mounted
27 on a slide by capillary action.
28

1 54. A combination as in claim 50, wherein said reagent
2 tray comprises a receptacle for an aliquot of a substance for
3 reaction with a sample, said receptacle having a surface/volume
4 ratio low enough to minimize evaporation of said substance.

5
6 55. A combination as in claim 50, wherein said reagent
7 tray comprises a receptacle for an aliquot of a substance for
8 reaction with a sample, said aliquot having a volume just large
9 enough to cover said sample mounted on a slide by capillary
10 action.

11
12 56. A combination as in claim 50, wherein said reagent
13 tray comprises a receptacle for an aliquot of a substance for
14 reaction with a sample, said receptacle having a volume just
15 large enough to receive a slide comprising said sample.

16
17 57. A combination as in claim 50, wherein
18 said reagent tray comprises a rectilinear external form
19 with said reagent tray lock coupled thereto;

20 said reagent tray is disposed for coupling to a first
21 one of said plurality of tiles, said first one tile having a tray
22 receptacle defining a rectilinear region into which said
23 rectilinear external form may just fit;

24 said receiving element a lock receptacle for receiving
25 said reagent tray lock, said lock receptacle defining a void
26 disposed near said rectilinear region into which said reagent
27 tray lock may just fit; and

28

1 said reagent tray lock is disposed to just fit into
2 said void when said reagent tray is just fit into said tray
3 receptacle.

4
5 58. A combination as in claim 57, wherein
6 said reagent tray lock comprises a spring member
7 coupled to said rectilinear external form, and a lip member
8 protruding from said rectilinear external form; and
9 said lip member is disposed to just fit into said void
10 when said reagent tray is just fit into said tray receptacle, and
11 said lip member is disposed to prevent release of said reagent
12 tray from said tile in response to a vertical force.

13
14 59. A combination as in claim 58, wherein
15 said reagent tray comprises a second member protruding
16 from said rectilinear external form;
17 said tray receptacle comprises a second receptacle for
18 receiving said second member, said second receptacle defining a
19 second void disposed near said rectilinear region into which said
20 second member may just fit;

21 said second member is disposed to just fit into said
22 second void when said reagent tray is just fit into said tray
23 receptacle; and

24 said reagent tray lock is disposed to allow release of
25 said reagent tray from said tile in response to horizontal force
26 combined with a vertical force.

1 60. In a system for performing a plurality of
2 independent analysis procedures simultaneously, each said
3 procedure having a sample and at least one process step for
4 operating on that sample, a data structure comprising a sequence
5 of process steps indexed by a time value and indicating a start
6 time and an end time for each said process step.

7
8 61. A data structure as in claim 60, comprising a
9 second sequence of process steps indexed by said time value,
10 wherein said second sequence comprises process steps from a
11 single procedure.

12
13 62. In a system for performing a plurality of
14 independent analysis procedures simultaneously, each said
15 procedure having a sample and at least one process step for
16 operating on that sample, a data structure comprising an ordered
17 sequence of entries, each said entry comprising a symbol on a
18 display screen and a process step.

19
20 63. A data structure as in claim 62, wherein each
21 entry comprises timing information for said process step.

22
23 64. In a system for performing a plurality of
24 independent analysis procedures simultaneously, each said
25 procedure having a sample and at least one process step for
26 operating on that sample, a device for coupling a robotic hand to
27 a slide holder, comprising

28

1 a first horizontal element defining a first hole
2 adapted to be coupled to said robotic hand;

3 a second horizontal element disposed above said first
4 horizontal element and adapted to restrain said first horizontal
5 element from motion in a vertical direction, and defining a
6 second hole;

7 a third horizontal element disposed below said first
8 horizontal element and adapted to restrain said first horizontal
9 element from motion in a vertical direction, and defining a third
10 hole;

11 said second hole disposed with at least some exposed
12 area that is not exposed by said first hole, and said third hole
13 disposed with at least some exposed area that is not exposed by
14 said first hole, whereby said first horizontal element is free to
15 move in response to coupling by said robotic hand.

16
17 65. A device as in claim 64, comprising a bumper
18 disposed above said first horizontal element.

19
20 66. A device as in claim 64, comprising a guiding
21 member coupled to said first horizontal element, whereby small
22 misalignments by said robotic hand cause said first horizontal
23 element to move in response to coupling by said robotic hand.

24
25 67. A device as in claim 66, wherein said guiding
26 member comprises a lip surrounding at least a part of said first
27 hole.

1 68. A device as in claim 64, comprising means for
2 coupling said second horizontal element to a frame.

3
4 69. A device as in claim 64, comprising means for
5 coupling said second horizontal element to said third horizontal
6 element, whereby said second horizontal element and said third
7 horizontal element define a space for disposing said first
8 horizontal element.

9
10 70. A device as in claim 64, wherein at least one of
11 said second and third holes is substantially elliptical.

12
13 71. A device as in claim 64, wherein said first hole
14 is substantially elliptical.

15
16 72. A device as in claim 64, wherein said first
17 horizontal element comprises a disk.

18
19 73. A device as in claim 64, wherein said first
20 horizontal element is substantially thinner than at least one of
21 said second horizontal element and said third horizontal element.

22
23 74. In a system for performing a plurality of
24 independent analysis procedures simultaneously, each said
25 procedure having a sample and at least one process step for
26 operating on that sample, a hydration fluid comprising less than
27 about 3% of a surfactant.

28

1 75. A hydration fluid as in claim 74, comprising about
2 .2% of said surfactant and about .1% of an acid.

3
4 76. A hydration fluid as in claim 74, comprising about
5 9980 milliliters water, about 20 milliliters tween, and about 10
6 grams sorbic acid, per 10 liters of fluid.

7
8 77. A hydration fluid as in claim 74, comprising less
9 than about 3% of an acid.

10
11 78. A hydration fluid as in claim 74, wherein said
12 surfactant is bridge or tween.

13
14 79. In a system for performing a plurality of
15 independent analysis procedures simultaneously, each said
16 procedure having a sample and at least one process step for
17 operating on that sample, an incubation oven element comprising
18 a hydration fluid supply;
19 an incubation chamber coupled to said hydration fluid
20 supply, said incubation chamber comprising a heat exchanger;
21 means for regulating an amount of said hydration fluid
22 applied to said sample; and
23 means for regulating a temperature applied to said
24 sample by said heat exchanger.

25
26 80. In a system for performing a plurality of
27 independent analysis procedures simultaneously, each said
28

1 procedure having a sample and at least one process step for
2 operating on that sample, a reagent tray comprising
3 a rectilinear external form with a reagent tray lock
4 coupled thereto;
5 said reagent tray lock disposed for coupling to a tile,
6 said tile being disposed at a selected location on a substrate in
7 said system;
8 said tile having a tray receptacle defining a
9 rectilinear region into which said rectilinear external form may
10 just fit;
11 said tray receptacle comprises a lock receptacle for
12 receiving said reagent tray lock, said lock receptacle defining a
13 void disposed near said rectilinear region into which said
14 reagent tray lock may just fit; and
15 said reagent tray lock is disposed to just fit into
16 said void when said reagent tray is just fit into said tray
17 receptacle.

18
19 81. A reagent tray as in claim 80, wherein
20 said reagent tray comprises a cover disposed thereon
21 with adhering means having sufficient power to prevent release of
22 said cover during normal handling and shipping, but able to
23 release said cover when said reagent tray is locked into said
24 tile with said reagent tray lock.

25
26 82. A reagent tray as in claim 80, wherein
27 said reagent tray comprises a plurality of receptacles,
28 each for an aliquot of a substance for reaction with said sample;

1 a first said receptacle and an second said receptacle
2 define a barrier disposed to prevent said substance from moving
3 from said first said receptacle to said second said receptacle
4 when said reagent tray is disposed in a first position, and
5 disposed to not prevent said substance from moving from said
6 first said receptacle to said second said receptacle when said
7 reagent tray is disposed in a second position.

8
9 83. A reagent tray as in claim 80, wherein
10 said reagent tray comprises a plurality of receptacles,
11 each for an aliquot of a substance for reaction with said sample;
12 a first said receptacle and an second said receptacle
13 define a barrier disposed to prevent said substance from moving
14 from said first said receptacle to said second said receptacle
15 when said reagent tray is disposed in a first position and said
16 aliquot is less than a selected amount, and disposed to not
17 prevent said substance from moving from said first said
18 receptacle to said second said receptacle when said reagent tray
19 is disposed in said first position and said aliquot is greater
20 than said selected amount.

21
22 84. A reagent tray as in claim 83, wherein said
23 selected amount is just large enough to cover said sample mounted
24 on a slide by capillary action.

25
26 85. A reagent tray as in claim 80, wherein
27 said reagent tray comprises a plurality of receptacles,
28 each for an aliquot of a substance for reaction with said sample;

1 said system comprises a sample holder having means for
2 holding a plurality of samples; and

3 each said receptacle is disposed to receive exactly one
4 of said plurality of samples coupled to a sample holder when said
5 sample holder is disposed adjacent to said tile.

6
7 86. A reagent tray as in claim 80, wherein said
8 reagent tray comprises a receptacle for an aliquot of a substance
9 for reaction with said sample, said receptacle having a
10 surface/volume ratio low enough to minimize evaporation of said
11 substance.

12
13 87. A reagent tray as in claim 80, wherein said
14 reagent tray comprises a receptacle for an aliquot of a substance
15 for reaction with said sample, said aliquot having a volume just
16 large enough to cover said sample mounted on a slide by capillary
17 action.

18
19 88. A reagent tray as in claim 80, wherein said
20 reagent tray comprises a receptacle for an aliquot of a substance
21 for reaction with said sample, said receptacle having a volume
22 just large enough to receive a slide comprising said sample.

23
24 89. A reagent tray as in claim 80, wherein
25 said reagent tray lock comprises a spring member
26 coupled to said rectilinear external form, and a lip member
27 protruding from said rectilinear external form; and

28

1 said lip member is disposed to just fit into said void
2 when said reagent tray is just fit into said tray receptacle, and
3 said lip member is disposed to prevent release of said reagent
4 tray from said tile in response to a vertical force.

5
6 90. A reagent tray as in claim 89, wherein
7 said reagent tray comprises a second member protruding
8 from said rectilinear external form;

9 said tray receptacle comprises a second receptacle for
10 receiving said second member, said second receptacle defining a
11 second void disposed near said rectilinear region into which said
12 second member may just fit;

13 said second member is disposed to just fit into said
14 second void when said reagent tray is just fit into said tray
15 receptacle; and

16 said reagent tray lock is disposed to allow release of
17 said reagent tray from said tile in response to horizontal force
18 combined with a vertical force.

19
20 91. In a system for performing a plurality of
21 independent analysis procedures simultaneously, each said
22 procedure having a sample and at least one process step for
23 operating on that sample, a workstation comprising
24 an incubation oven element comprising a hydration fluid
25 supply, an incubation chamber coupled to said hydration fluid
26 supply, said incubation chamber comprising a heat exchanger
27 having a plurality of heat exchanger elements disposed in an
28 array, means for regulating an amount of said hydration fluid

1 applied to said sample, and means for regulating a temperature
2 applied to said sample by said heat exchanger; and
3 a slide holder adapted for disposition at said
4 incubation oven element, said slide holder comprising a set of
5 slides disposed in an array matched to said heat exchanger
6 element.

7
8 92. A workstation as in claim 91, comprising means for
9 cooling said incubation chamber while said slides are disposed
10 therein.

11
12 93. A workstation as in claim 92, wherein said means
13 for cooling comprises a fan and a temperature regulator coupled
14 thereto.

15
16 94. A workstation as in claim 91, comprising means for
17 isolating said heat exchanger elements from said hydration fluid.

18
19 95. A workstation as in claim 91, comprising one said
20 heat exchanger element for each pair of said slides.

21
22 96. A workstation as in claim 91, wherein said heat
23 exchanger elements comprise fins adapted to be disposed near to
24 said samples on said slides.

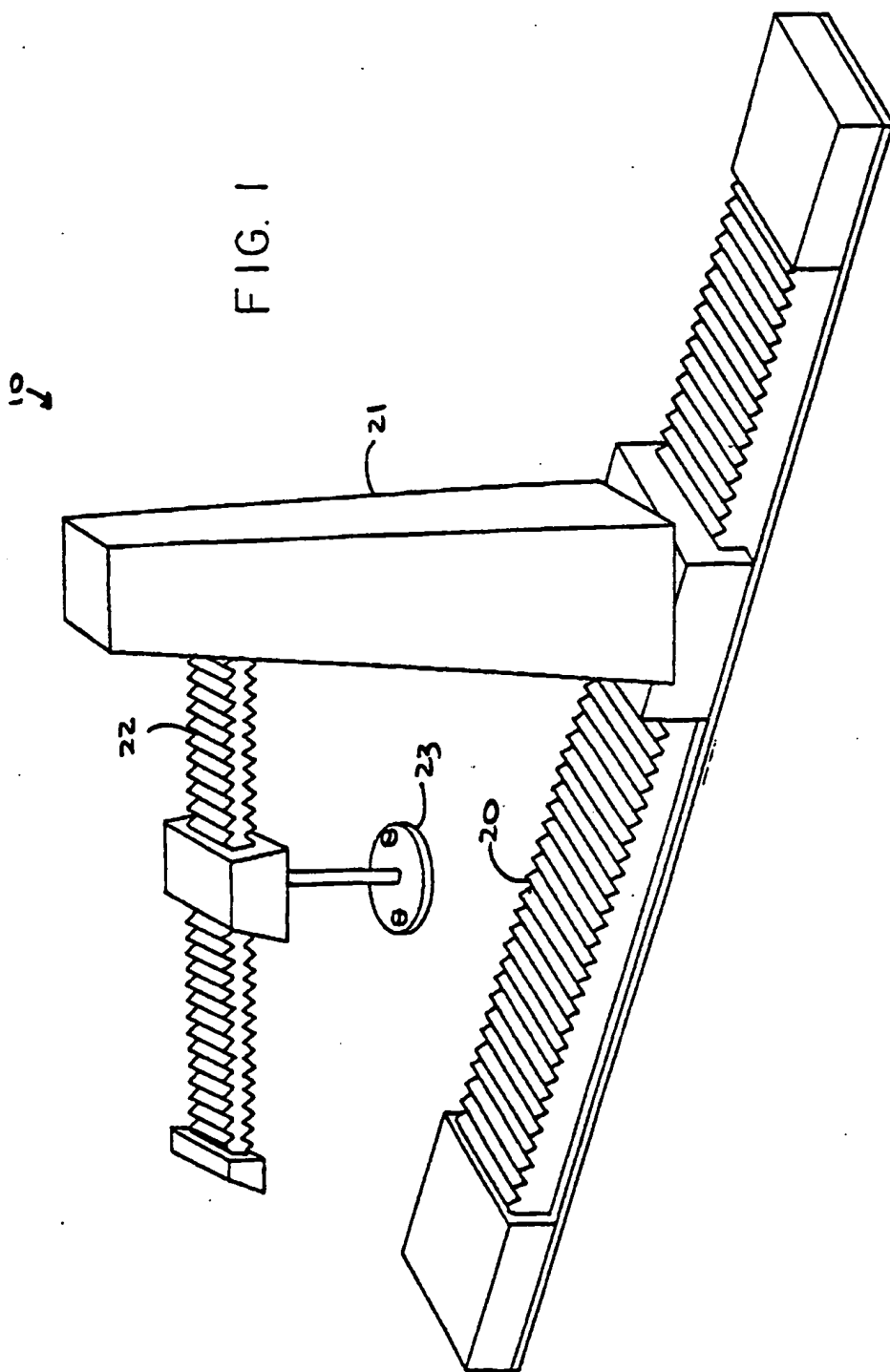
25
26 97. A workstation as in claim 91, wherein said means
27 for regulating an amount of said hydration fluid comprises
28 a fluid well coupled to said incubation chamber; and

1 means for maintaining a level of hydration fluid in
2 said fluid well at a selected level.

3
4 98. A workstation as in claim 91, wherein said means
5 for regulating a temperature comprises means for cooling said
6 incubation chamber.

7
8 99. A workstation as in claim 91, wherein said slide
9 holder comprises a slide cover having a set of adjustable
10 ventilation openings.

11
12 100. A workstation as in claim 91, wherein said slide
13 holder comprises a V shaped structural member disposed to direct
14 condensation away from a set of slides.



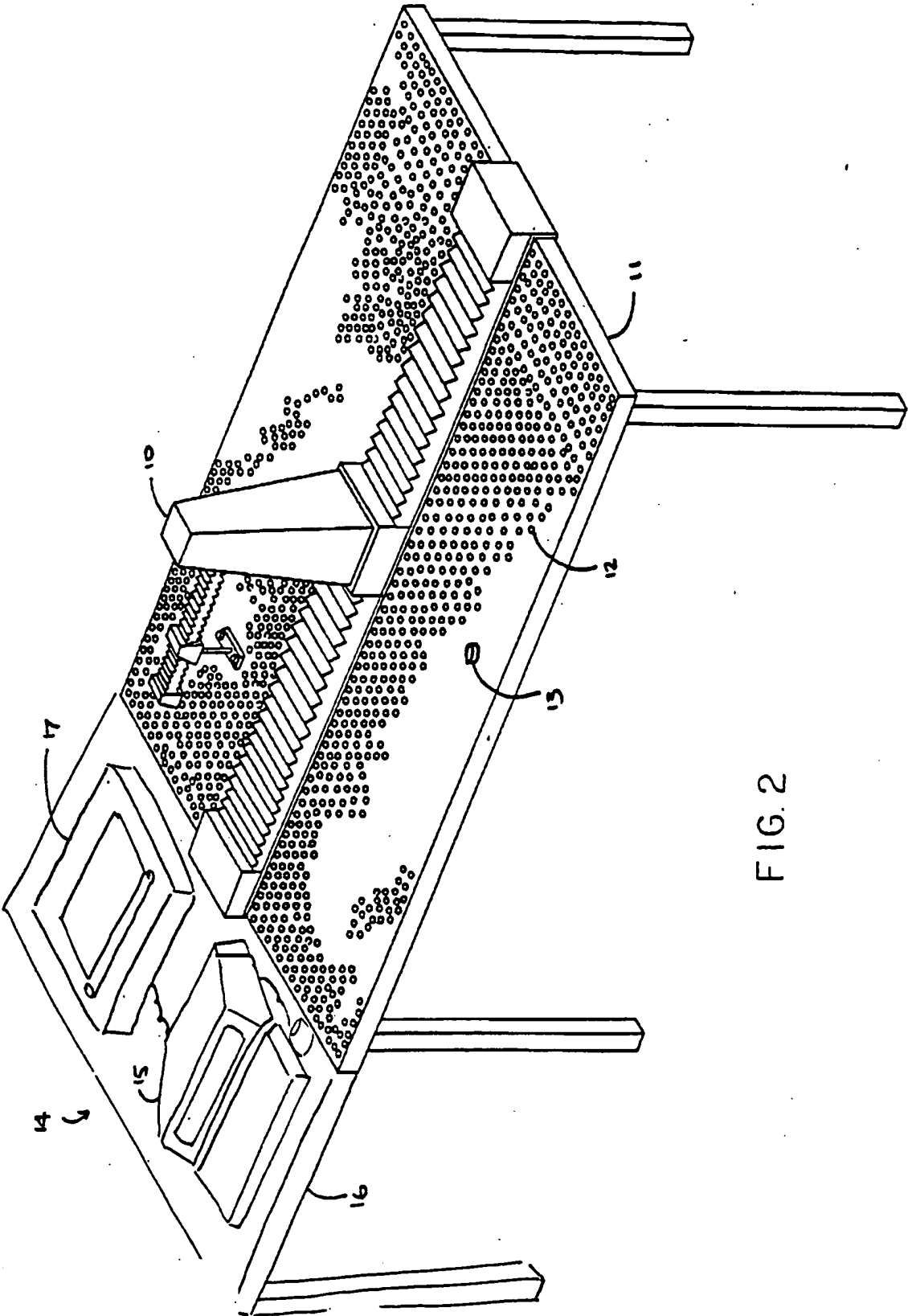


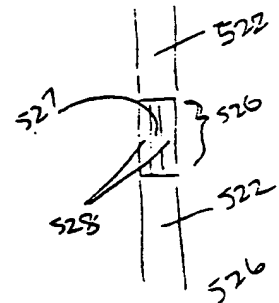
FIG. 2

4

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figure
38-1

D

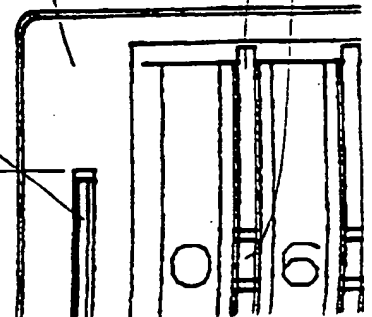
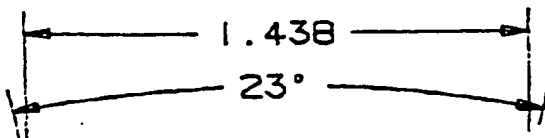


422

522

423

.546 REF



2

LTR	DES
1	PREPRO
2	ADDED NU
A	REV'D TO

24 PT HELVETICA BOLD
.010 HIGH-MATTE FINISH
CENTER AS SHOWN

462

420

R .050

466

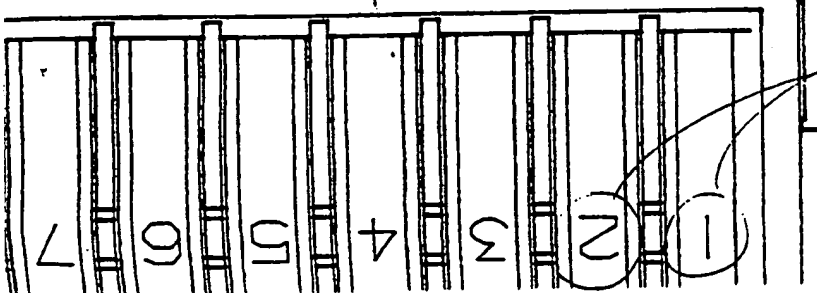


figure
5B-2

33-1	33-2	33-3
33-4	33-5	33-6

figure 33

REVISIONS				
ON	ECO NO.	BY	DATE	APPROVED
ION REL		SFB	6-25-92	
R.020 I-C		SFB	7-9-92	
NT DESIGN		SFB	2-19-93	

D

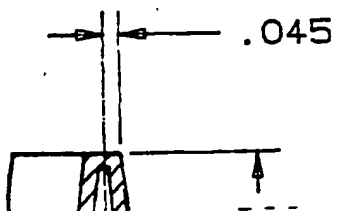
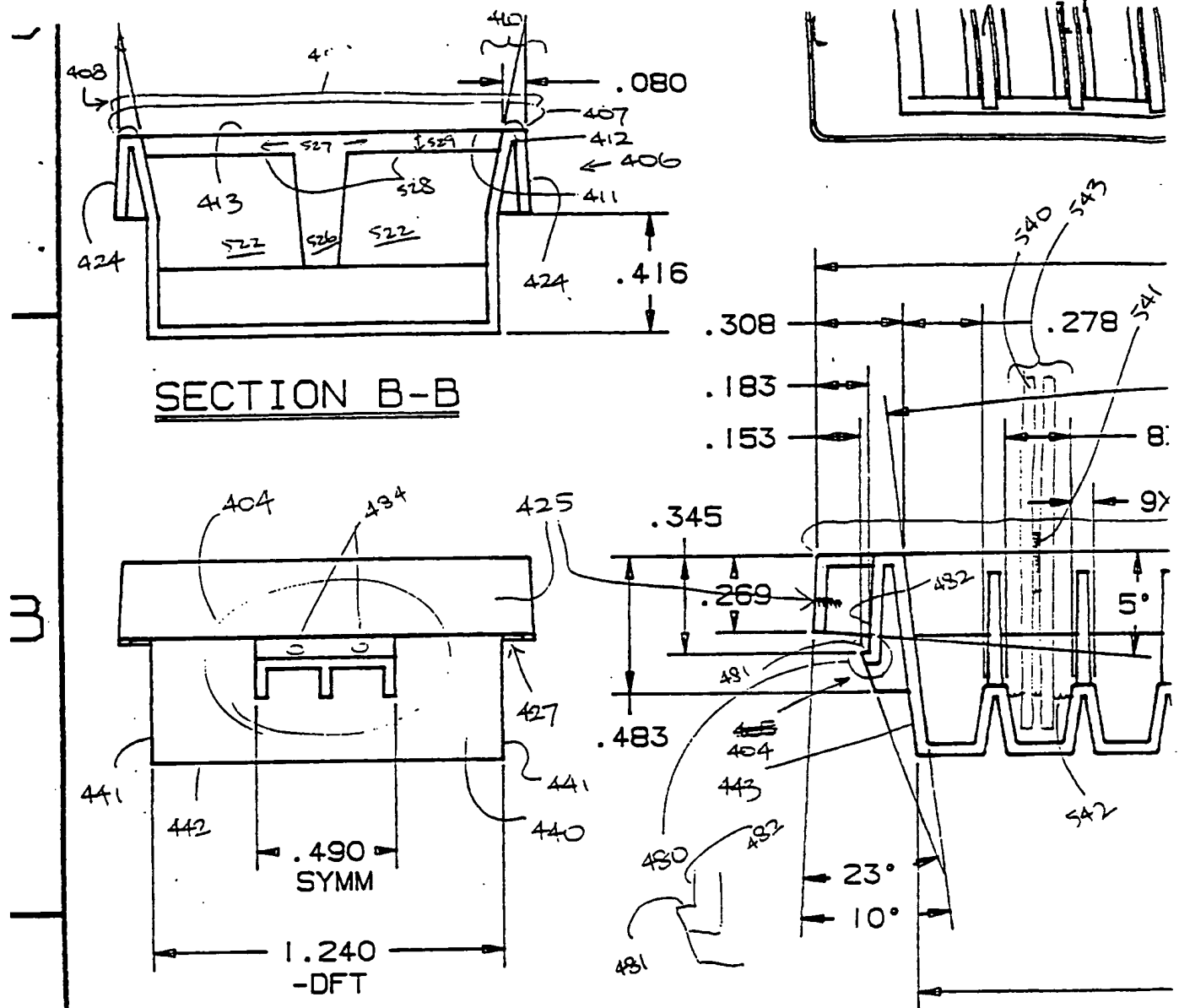


figure
33-33



1. WALL THICKNESS .040
2. FILLETS AND RADII R.010
3. DRAFT $1/2^\circ$ MAX

figure
33-4

NOTES: UNLESS OTHERWISE SPECIFIED

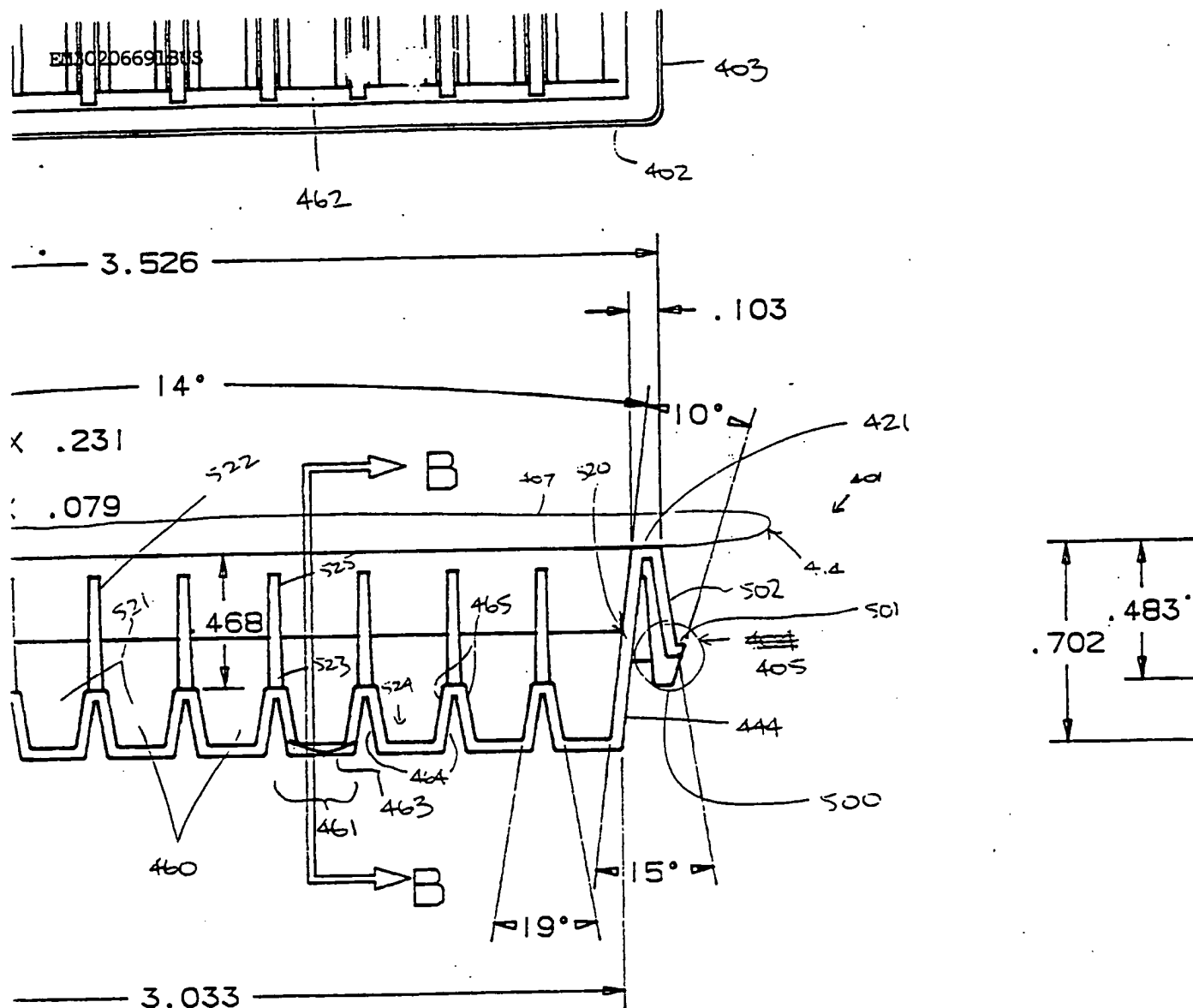
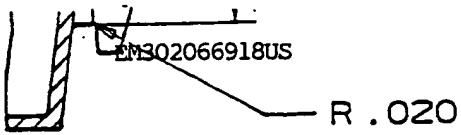


figure
3B-5

MATERIAL	TOLERANCES UNLESS OTHERWISE SPECIFIED DIMENSIONS ARE IN INCHES TOLERANCES 125 ✓ .X ±.1 .XX ±.02 .XXX ±.005 MACH. SURF. ✓ ANGULAR 40° 30'	QTY PER ASSY APPROVALS DRAWN ENGR S BARKER APPD
FINISH	THREADS, CLASS 2A OR 2B REMOVE BURRS & SHARP EDGES .020 MAX. MACH. FILLET RADIUS .020 MAX. MACH. SURF. FLAT WITHIN .001 IN./IN. OTHER SURF. FLAT WITHIN .005 IN./IN. CONCENTRICITY MACH. SURF. T.I.R. WITHIN 1/2 SUM OF DIAS. TOL. .001 MIN.	DO NOT SCALE DR



SECTION A-A

IB TYP 2 PLCS

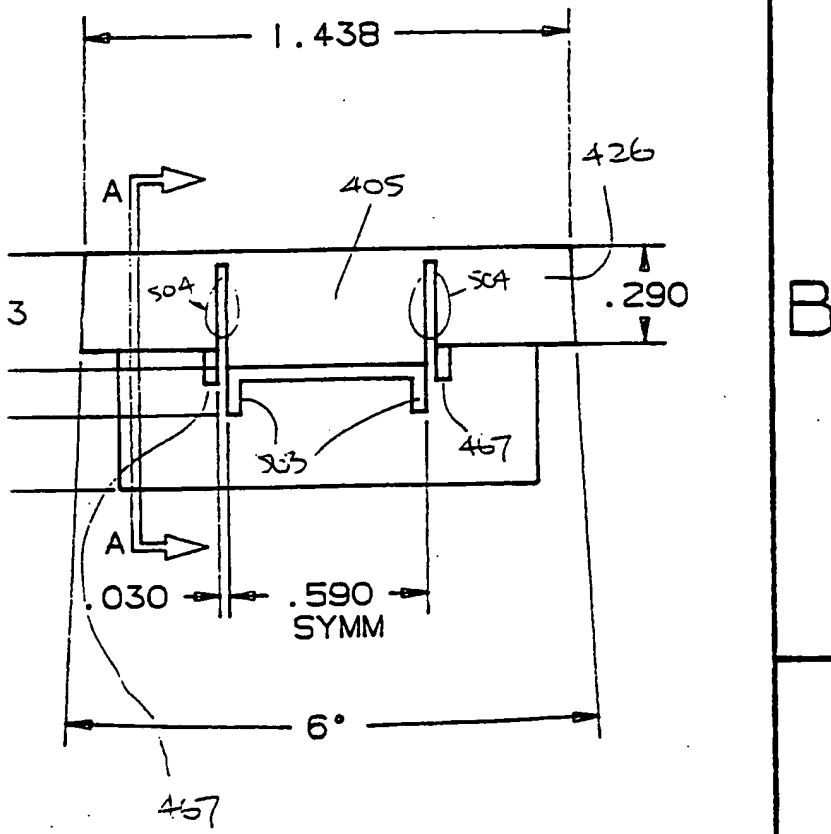


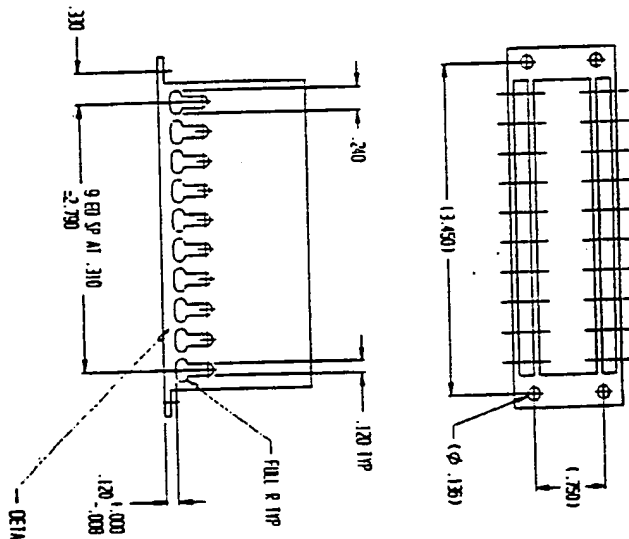
figure
33-6

BIOTEK SOLUTIONS			
E	TITLE DISPOSABLE, 10 WELL		
32	SIZE C	DWG. NO. 100508	REV. A
NG	SCALE 2X	SHEET 1	OF 1

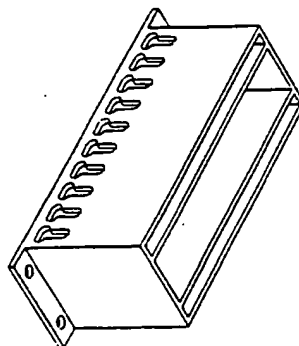
FIG. 3C-3, P. 1

NOTES: UNLESS OTHERWISE SPECIFIED

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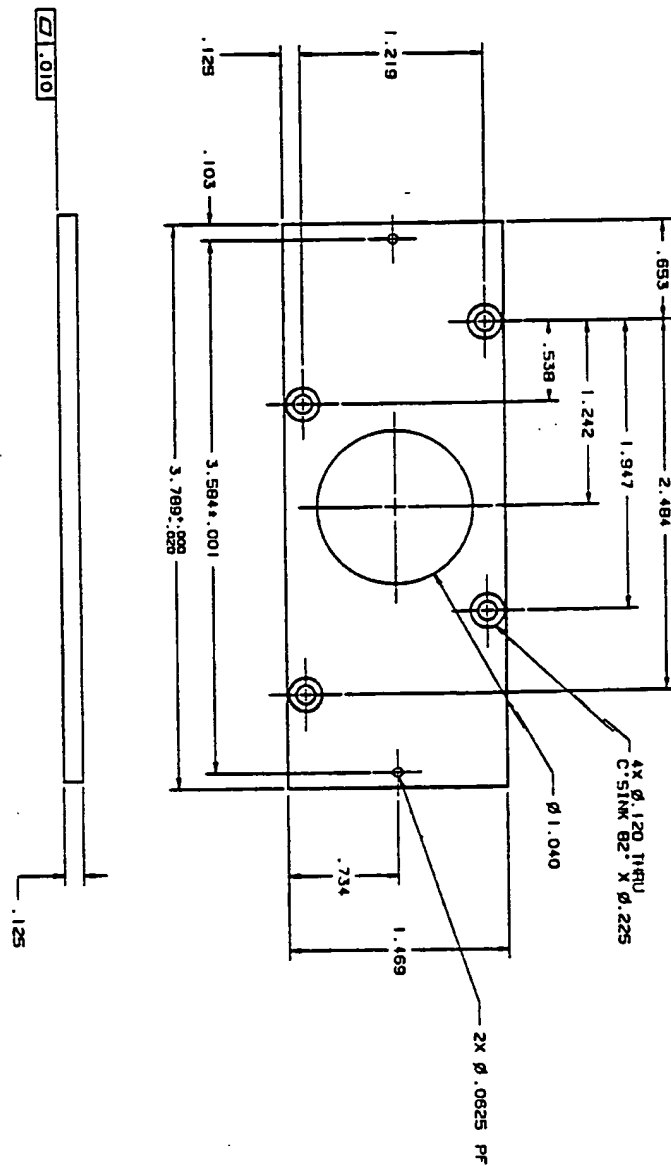
REVISIONS		
REV	DESCRIPTION	DATE
1	PREPRODUCTION REL	12-3-92
2	1.20WOS.100 .240WOS.200	12-4-94



MATERIAL		TOLERANCES		UNITS		DATE		Biotech Solutions Inc	
FINISH		UNLESS OTHERWISE SPECIFIED		3		5-94		MOD, SLIDE HOLDER	
		DECIMALS		FRACTIONS		DATE		REV	
		1/16		1/32		12-92		1	
		1/8		1/16				2	
		3/16		1/8					
		1/2		3/16					
		5/8		1/2					
		1		5/8					
		1 1/8		3/4					
		1 1/4		7/8					
		1 1/2		1					
		1 3/4		1 1/8					
		2		1 1/4					
		2 1/2		1 3/8					
		3		1 1/2					
		3 1/2		1 5/8					
		4		1 3/4					
		4 1/2		1 7/8					
		5		2					
		5 1/2		2 1/8					
		6		2 1/4					
		6 1/2		2 3/8					
		7		2 1/2					
		7 1/2		2 5/8					
		8		2 3/4					
		8 1/2		2 7/8					
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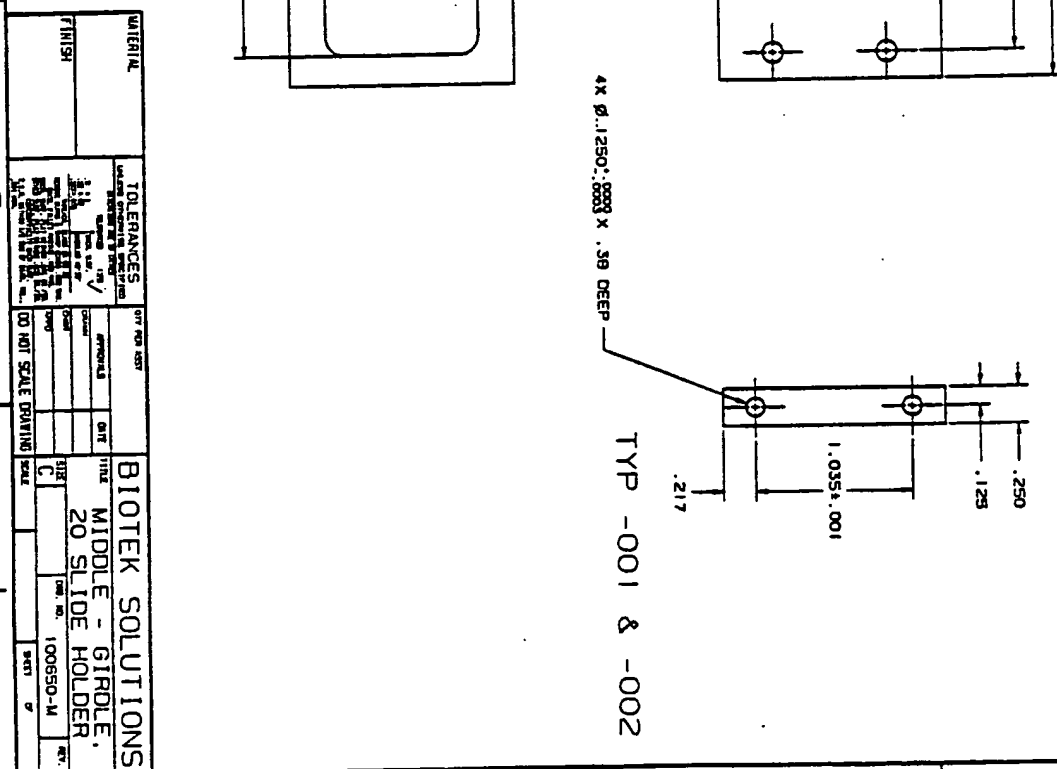
FIG. 3C-3, P. 2

NOTES: UNLESS OTHERWISE SPECIFIED

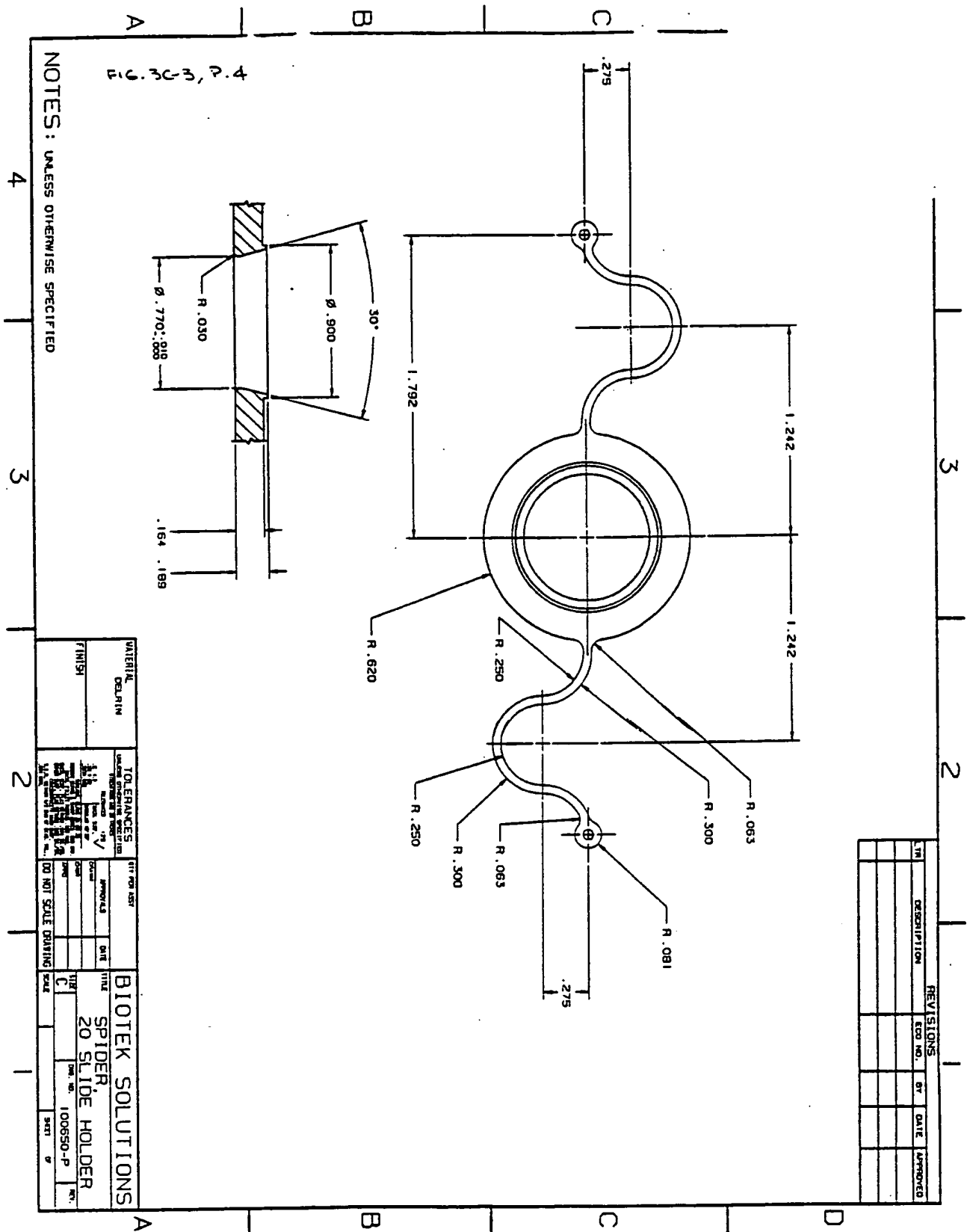


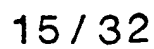
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FINISH		APPROVALS		DATE	
DO NOT SCALE DRAWING		TITLE		DATE	
		COVER		100650-C	
		20 SLIDE HOLDER		100650-C	
		100650-C		100650-C	

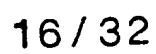
REVISIONS		REV. NO.		DATE		APPROVED	
1	DESCRIPTION	ECO NO.	BT	DATE	APPROVED		



REVISIONS					
LIN	DESCRIPTION	ECO NO.	BY	DATE	APPROVED







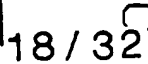
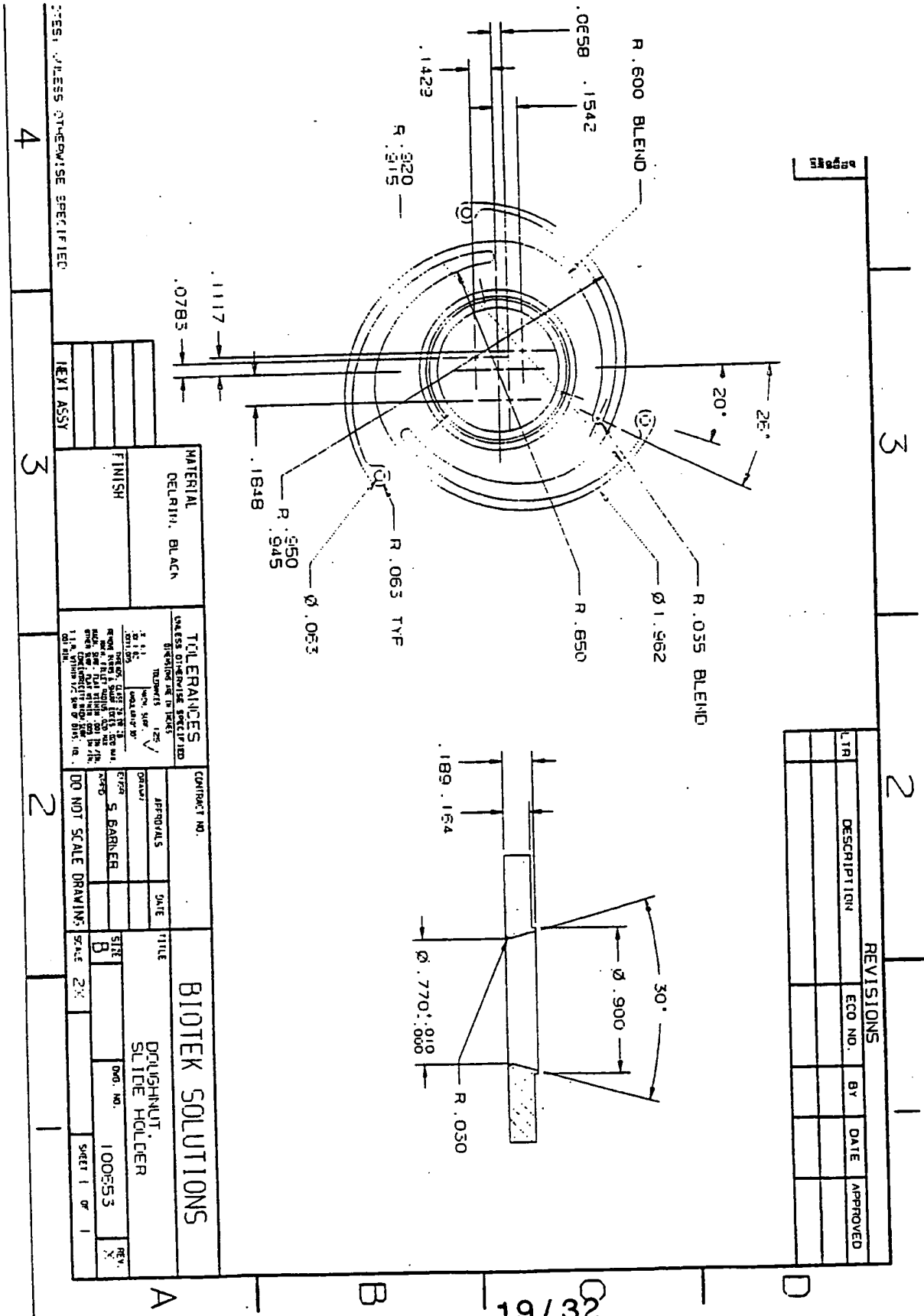


Fig. 3C-3,



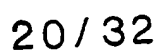
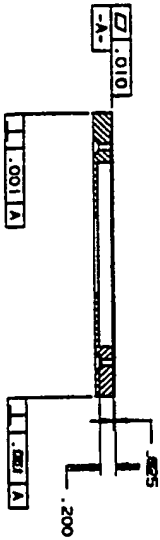
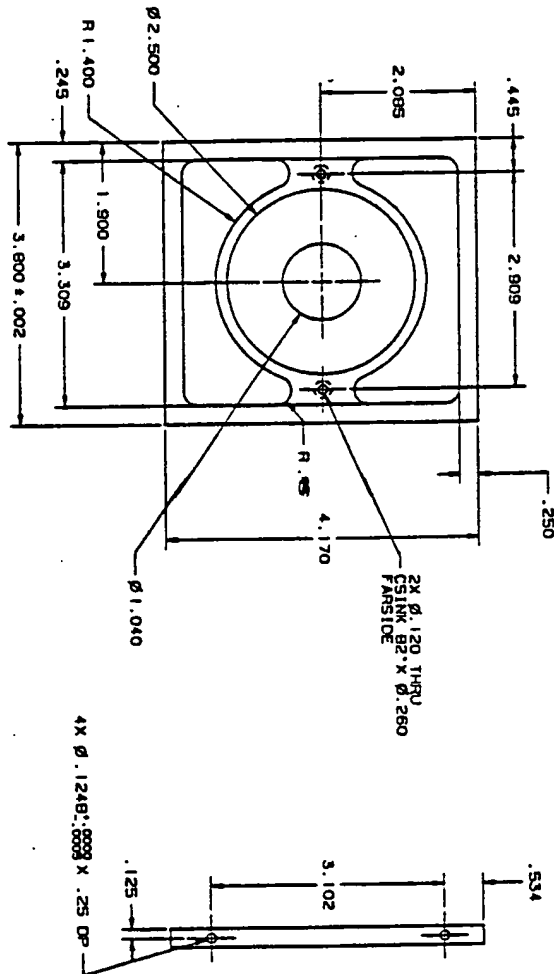


FIG. 3C-3, P. 11.

NOTES: UNLESS OTHERWISE SPECIFIED



REV. STIONS			
TR	DESCRIPTION	EQ. NO.	DATE
A	PRODUCTION REL.	SFB 4-29-92	
B	REVISED WIDTH	SFB 5-20-92	
C	Ø.120 was 2-56UNC	SFB 8-18-92	
D	REMOVED PINS	SFB 8-1-92	

MATERIAL		TOLERANCES		CONTACT NO.	
KOB-18 ALUM. 1.500 THK		FRACTIONAL DECIMAL MILS THICKNESS TOLERANCE		BIOTEK SOLUTIONS	
FINISH		APPROVALS		DATE	
WIND ANODIZE CLEAN		DESIGNED BY S. DAVEN		3-92	
NEXT ASSY		CHECKED BY C		100656	
		DO NOT SCALE DRAWING		1X	
				TOP PLATE SLIDE HOLDER	
				REV. D	



FIG. 3C-3, p. 13.

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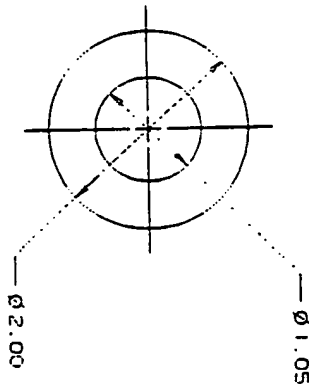
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REVISIONS

REVISIONS					
LTR	DESCRIPTION	ECO NO.	BY	DATE	APPROVED
A	PRODUCTION REL		SFB	12-14-92	
B	KOLLSMAI RELEASE		SFB	12-14-93	

It may be possible to
 obtain a grant to
 build a building
 on the land on
 a temporary basis as
 the white matter



NOTES: UNLESS OTHERWISE SPECIFIED

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BIOTEK SOLUTIONS

MATERIAL
SILICONE SHEET
McMASTER CARR
P11 B522N31

TOLERANCES

0:00 PM A-55

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[illegible]

NO SCALE DRAWINGS

SCALE FULL

[illegible]

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FIG. 3D-1

TechMate™ Incubation Oven

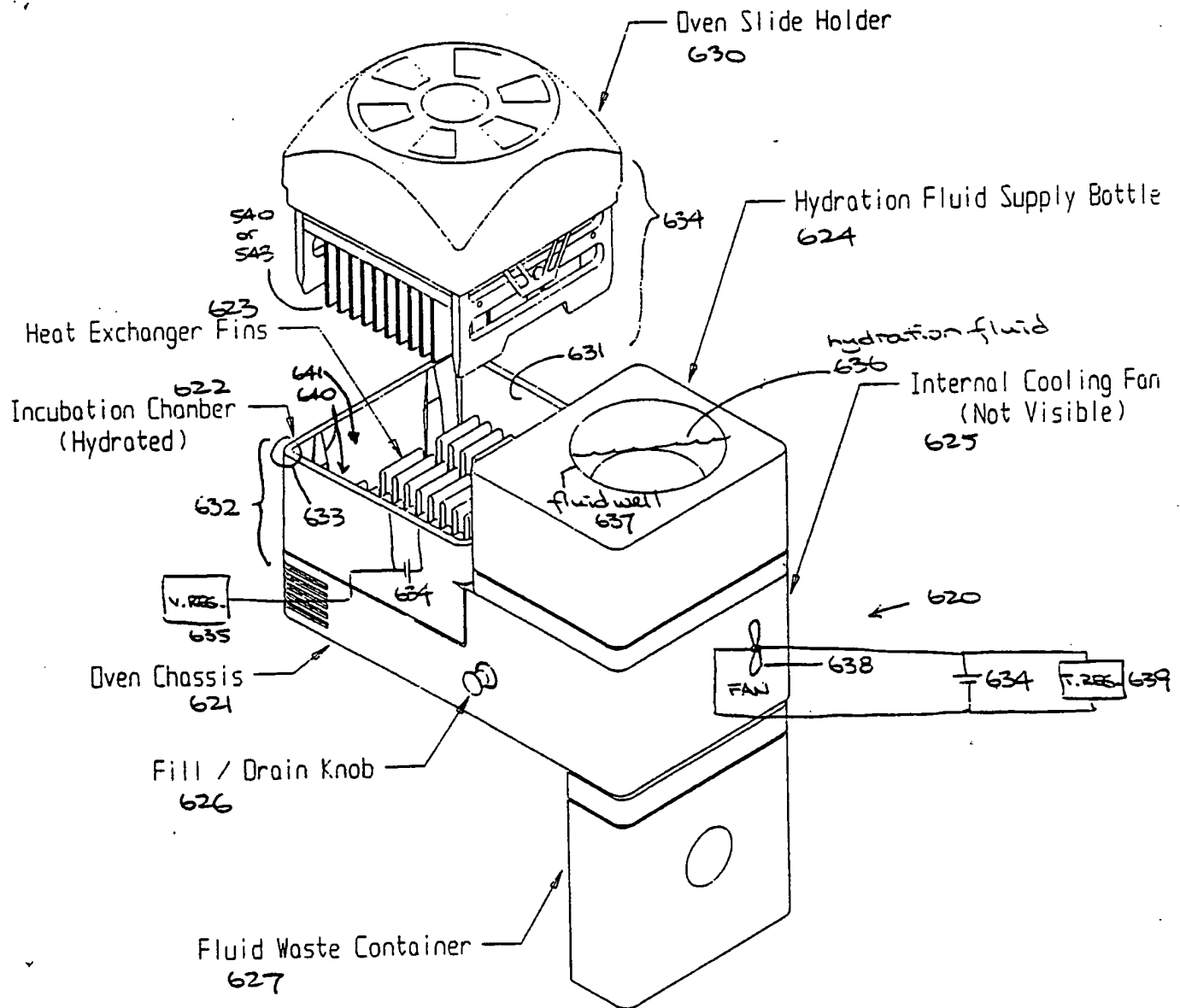
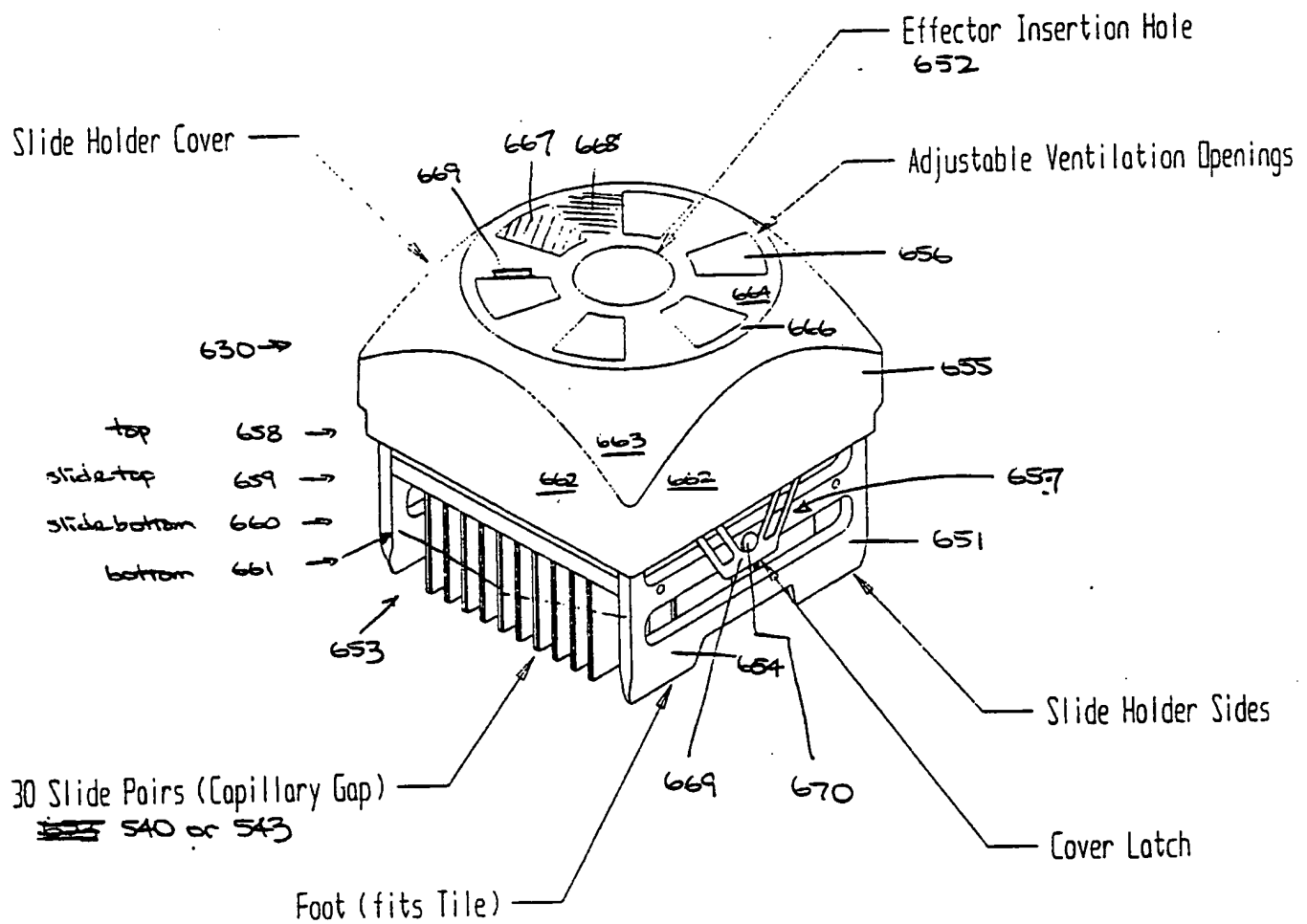


FIG. 3D-2

TechMateTM Oven Slider Holder



WIRE 3E

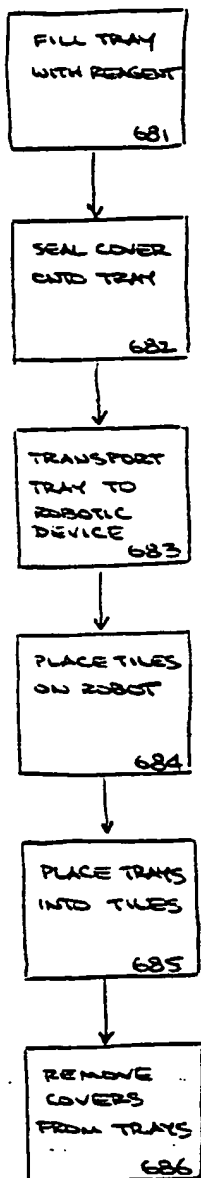


FIG. 4

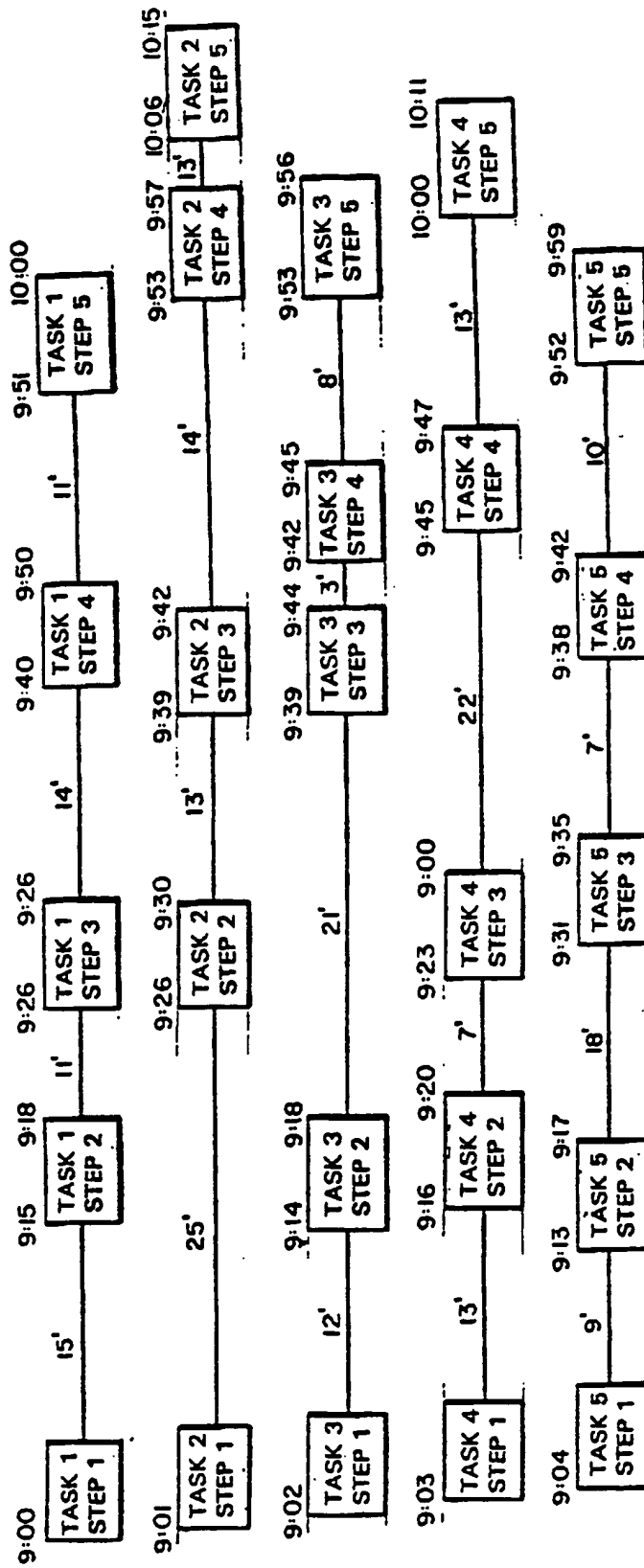


FIG. 5

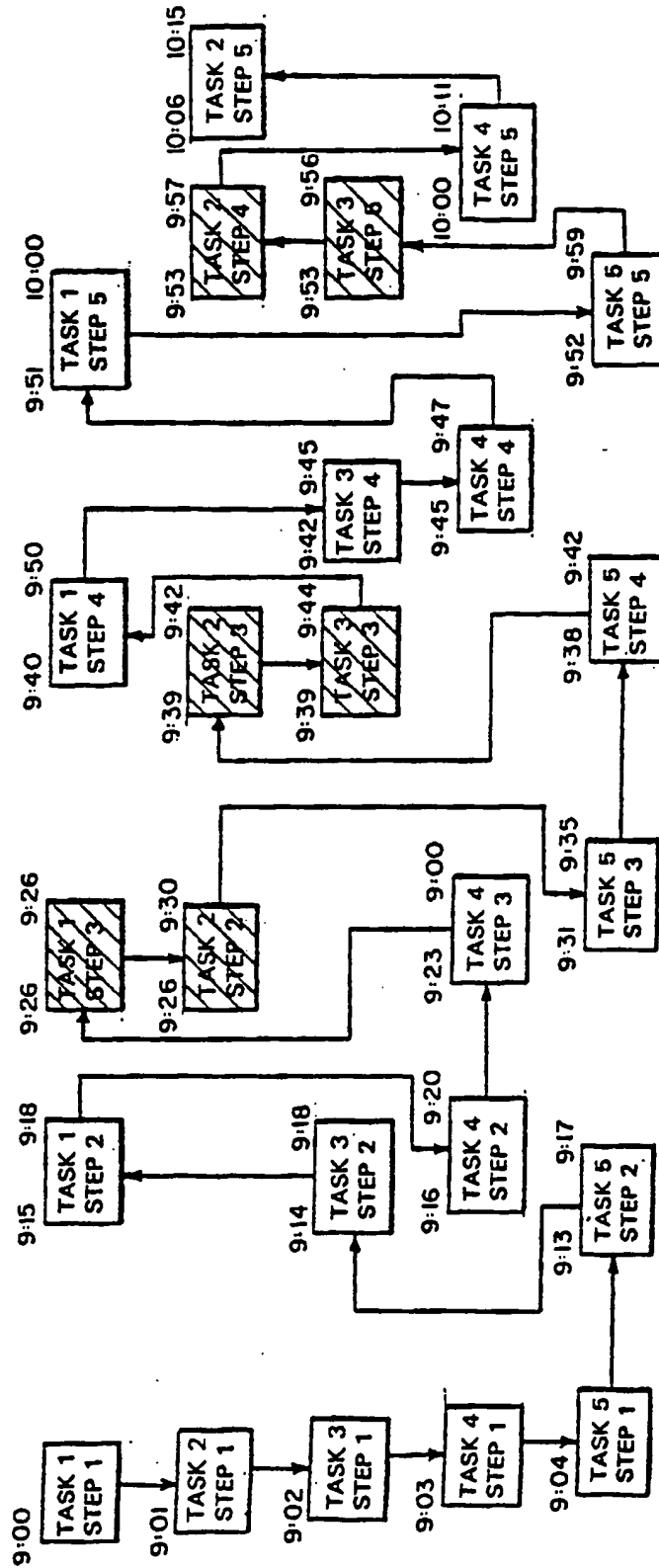


Figure 6.

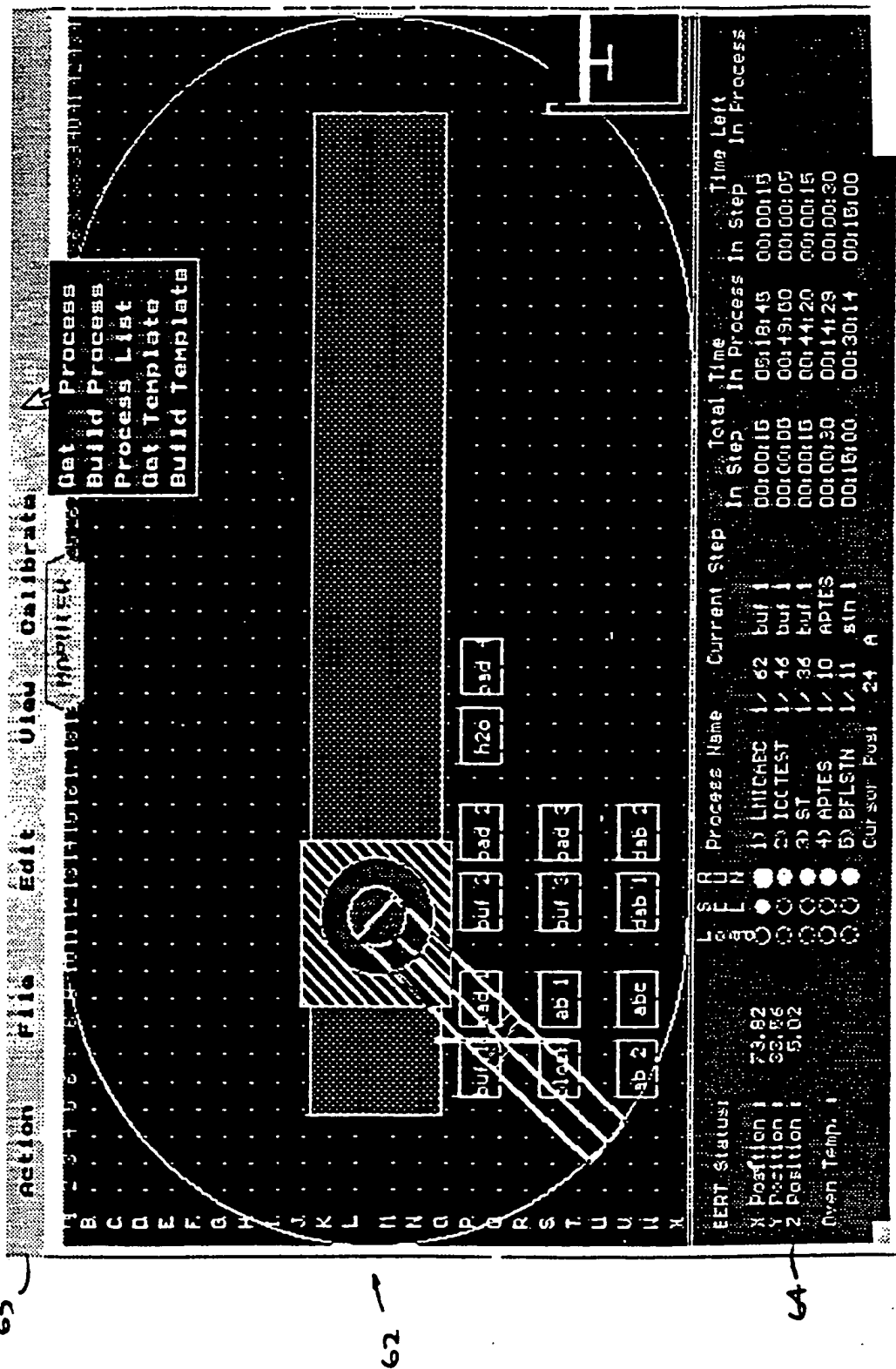


Figure 7.

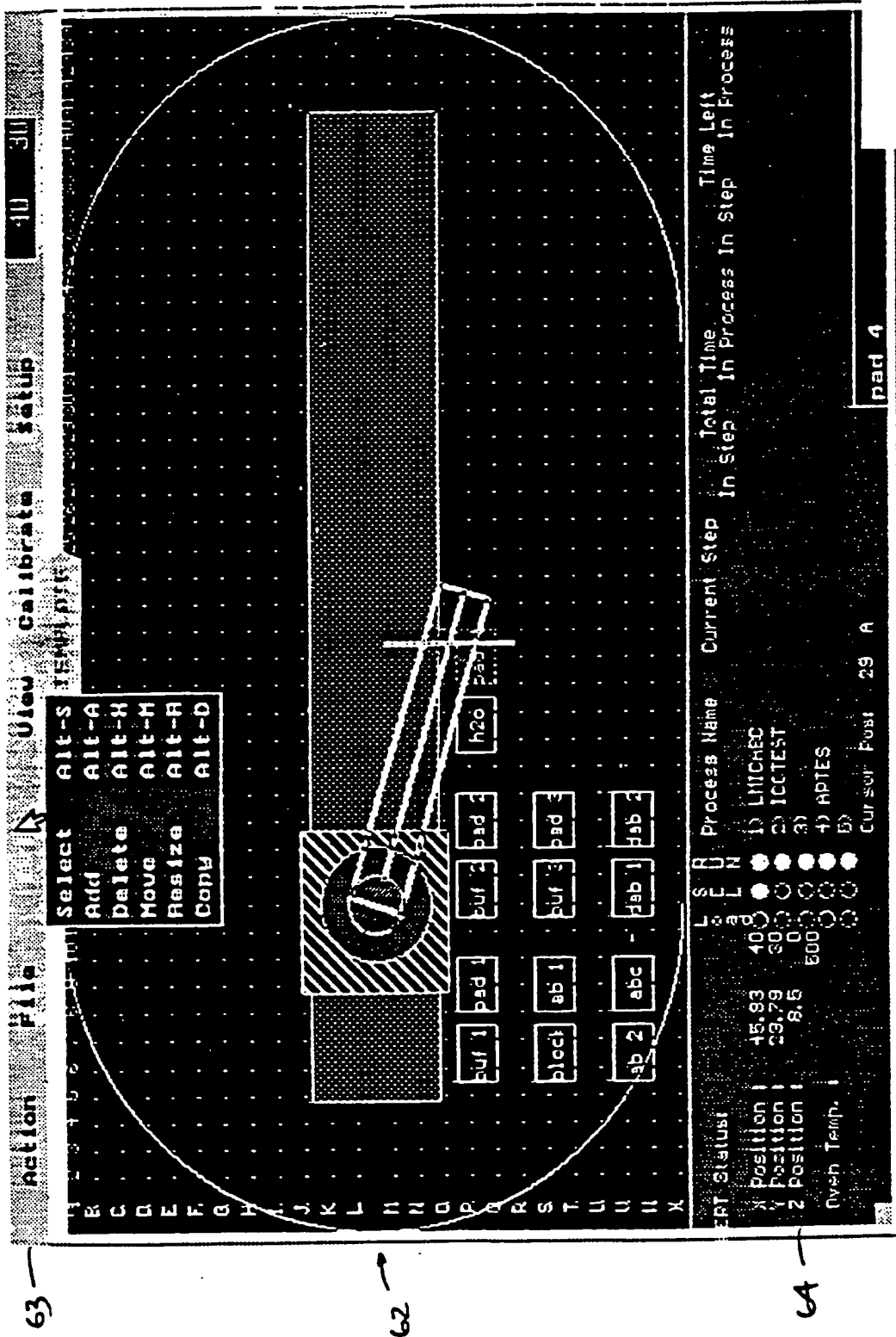


Figure 8.

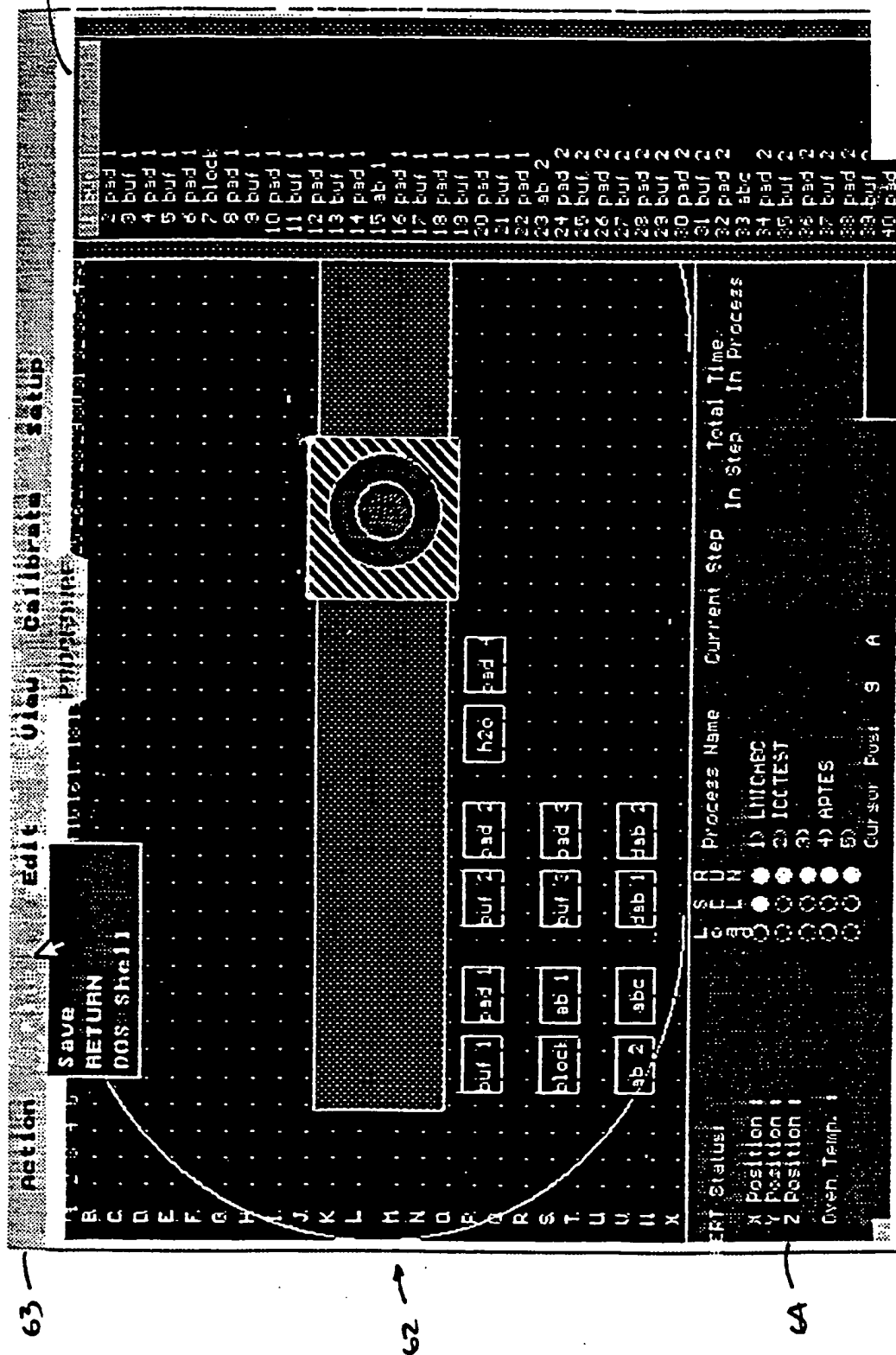


Figure 9.

Action	File	Edit	Utau	Calibrate	Status	Progress	Unit
Step No.	Step Name	Min Time	Max Time	Yes/No/Hold			
1	huf 1	00:00:15	00:05:00	No			
2	pad 1	00:00:30	00:00:30	Yes			
3	huf 1	00:00:15	00:05:00	No			
4	pad 1	00:00:30	00:00:30	No			
5	huf 1	00:00:15	00:05:00	Yes			
6	pad 1	00:00:30	00:00:30	Yes			
7	block	00:30:00	00:30:00	Yes			
8	pad 1	00:00:30	00:00:30	Yes			
9	huf 1	00:00:15	00:05:00	Yes			
10	pad 1	00:00:30	00:00:30	Yes			
11	huf 1	00:00:15	00:05:00	Hold			
12	pad 1	00:00:30	00:00:30	Yes			
13	huf 1	00:00:15	00:05:00	Yes			
14	pad 1	00:00:30	00:00:30	Yes			
15	ab 1	02:00:00	02:00:00	Yes			
16	pad 1	00:00:30	00:00:30	Yes			
17	huf 1	00:00:15	00:05:00	Yes			
18	pad 1	00:00:30	00:00:30	Yes			
19	huf 1	00:00:15	00:05:00	Yes			
20	pad 1	00:00:30	00:00:30	Hold			
21	huf 1	00:00:15	00:05:00	Yes			
22	pad 1	00:00:30	00:00:30	Yes			
23	ab 2	00:45:00	00:45:00	Yes			
24	pad 2	00:00:30	00:00:30	Yes			
25	huf 2	00:00:15	00:05:00	Yes			

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/06156

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 219/521, 525, 531; 395/82, 88, 92, 99; 422/50, 63, 102; 436/43, 46, 47, 518

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	J. Chem. Inf. Comput. Sci., Vol. 28, No. 4, 1988, T.L. Isenhour and P.B. Harrington, "TORTS: An Expert System for Temporal Optimization of Robotic Procedures," pp. 215-21.	19, 20, 23, 24, 28, 29, 30, 47
X	Rev. Sci. Instrum., Vol. 6, No. 6, June 1988, J.S. Lindsey et al., "Robotic work station for microscale synthetic chemistry: On-line absorption spectroscopy, quantitative automated thin-layer chromatography, and multiple reactions in parallel," pp. 940-950, especially section I. System Description.	22
A	Hudson Control Group, Inc., Software Product Specification, "Total Control for Windows" Data Sources Report, (V. 1.1), December 1994.	1-3, 17-48

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A		document defining the general state of the art which is not considered to be part of particular relevance
*E		earlier document published on or after the international filing date
*L		document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
*O		document referring to an oral disclosure, use, exhibition or other means
*P		document published prior to the international filing date but later than the priority date claimed
	*X	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
	*Y	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
	*G	document member of the same patent family

Date of the actual completion of the international search

29 SEPTEMBER 1995

Date of mailing of the international search report

24 OCT 1995

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer
Robert Downs
ROBERT DOWNS

Telephone No. (703) 305-9642

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/06156

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Analytical Chemistry, Vo. 54, No. 13, November 1982, G.D. Owens and R.J. Eckstein, "Robotic Sample Preparation Station," pp. 2347-2351.	1-3, 17-48, 64-73
A	Hewlett-Packard Journal, Vol. 44, No. 3, June 1993, G.B. Gordon et al., "ORCA: optimized robot for chemical analysis," pp. 6(14).	1-3, 17-48
A	US, A, 4,727,494 (BUOTE) 23 February 1988.	1-3, 17-48
A	US, A, 4,835,711 (HUTCHINS et al.) 30 May 1989.	1-3, 17-48
A	US, A, 4,843,566 (GORDON et al.) 27 June 1989.	1-3, 17-48
A	US, A, 4,087,248 (MILES) 02 May 1978.	1-3, 17-48
A	US, A, 5,229,074 (HEATH et al.) 20 July 1993.	1-3, 17-48
A,P	US, A, 5,355,304 (DEMORANVILLE et al.) 11 October 1994.	1-3, 17-48
X	US, A, 5,016,170 (POLLALIS et al.) 14 May 1991, see entire document.	4-6, 60-63
A	US, A, 4,495,149 (TWATA et al.) 22 January 1985, columns 13-14.	7, 49
X	US, A, 5,281,394 (HOLUB) 25 January 1994, column 7, line 57 to column 8, line 30.	80, 82, 83, 89, 90
A		33-46, 50-59
A	US, A, 4,952,518 (JOHNSON et al.) 28 August 1990, column 9, lines 36-40.	7, 49-59
A	US, A, 4,719,087 (HANAWAY) 12 January 1988, column 8, lines 32-39.	33-46, 80-90
X	US, A, 4,384,193 (KLEDZIK et al.) 17 May 1983.	8, 79, 91, 94, 95
X	US, A, 5,225,325 (MILLER et al.) 06 July 1993, column 16, lines 1-5.	74, 78
Y	US, A, 5,037,484 (SU et al.) 06 August 1991, column 3, lines 18-28.	74-78

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/06156

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 4,929,619 (BLACKMAN) 29 May 1990, column 5, line 43 to column 6, line 40.	74-78

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/06156

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☒ No protest accompanied the payment of additional search fees.